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A CRITIQUE OF PROPOSED "IDEAL" STERILIZATION LEGISLATION

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This paper does not concern itself with sterilization as a rational, well thought out measure, applicable to individual cases of feeblemindedness and mental disease. Personal researches concerning the hereditary factor in mental diseases and mental defects have led to the logical conclusion that from the biologic standpoint there are persons who should be sterilized in order that their particular type of mental disease or defect shall not be transmitted to succeeding generations. Whatever may be the theological or legal attitudes toward such psychiatric situations, the psychiatrist, as one whose point of view is biologic, must agree that a limited program of sterilization is eugenically sound. Whether such a program would be practical, or whether it would override legal rights, which are to a certain extent as important as biologic rights, is not a matter for consideration in this study.

In thirty states of the Union, from the date of the first law till Dec. 1, 1931, a total of about 15,162 sterilizations were performed; by far the larger part were performed on inmates of institutions, mainly of institutions for the insane and the feebleminded, and in many cases the person submitted voluntarily to the procedure. It is not probable, however, that such sterilizations can have an appreciable effect on the number of feebleminded and insane persons.

I therefore state that I am in sympathy with limited sterilization laws. This article specifically attacks as extravagant and as approaching mania a proposed sterilization law set up as the ideal by certain important eugenists. The fact that this proposed law seems to have little chance of being accepted by many American communities does not make this paper superfluous. What will be accepted by any community is unpredictable, as the whole world has witnessed in the recent developments, in social and legal matters here and abroad. Incredible laws have a way of getting into action through the persistent efforts of those who aim to seize the power in a community.

This article, therefore, may be considered as antipropaganda. Moreover, any one who wishes for rational eugenic measures to become operative must fight irrational measures, since it frequently happens that the

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overenthusiastic proponents of a cause hurt it more than do its enemies, as is well epitomized in the popular proverb: "God save me from my friends; I can look after my enemies myself." Eugenics is, in my opinion, being made ridiculous as well as a threat to civilized life by the law under consideration.

I intend to discuss the proposed "ideal" legislation and, further, to uncover the philosophy of life, the attitude toward freedom and individuality, expressed in the latest writings of the leaders of the group which advocates this legislation. Ideal legislation should spring from certainty of knowledge, from facts accepted by the bulk of biologists and geneticists. If one examines, however, the writings of important workers in the field of biology, psychiatry and eugenics, one finds no justification whatever for the proposed program.

I shall now cite from an authoritative monograph, "The Legal Status of Eugenical Sterilization" by Dr. H. H. Laughlin.[1] Dr. Laughlin's position is established by his connection with the Eugenics Record Office of the Carnegie Institution of Washington and by his secretaryship of the board of editors of the *Eugenical News,* which is the organ of the Galton Society and of the Third International Congress of Eugenics and is published for the Eugenic Research Association at Cold Spring Harbor, Long Island, N. Y.

In this monograph Dr. Laughlin discussed at great length the litigation under the Virginia sterilization statute which led to the notable decision of the Supreme Court of the United States upholding the statute, and he then proposed certain ideal legislation. His "Draft A" is the full text for a detailed sterilization law which starts out as a declaration of purpose:

> An Act to prevent the procreation of persons socially inadequate from defective inheritance, by authorizing and providing for the eugenical sterilization of certain potential parents carrying degenerate qualities.

In order to make clear who these persons are and how they should be found, Dr. Laughlin gave certain definitions. He stated:

> A socially inadequate person is one who by his or her own effort, regardless of etiology or prognosis, fails chronically, in comparison with normal persons, to maintain himself or herself as a useful member of the organized social life of the state, provided that the term socially inadequate shall not be applied to any person whose individual or social ineffectiveness is due to the normally expected exigencies of youth, old age, curable injuries, or temporary physical or mental illness, *in case such ineffectiveness is adequately taken care of by the particular family in which it occurs* [italics mine].

1. No attempt is made here to give a complete bibliography on sterilization. The "ideal" sterilization law is contained in the monograph, "The Legal Status of Eugenical Sterilization," by Harry H. Laughlin, a supplement to the annual report of the Municipal Court of Chicago for the year 1929. This is a valuable document for many reasons.

I call attention to the fact that in some of the definitions there occurs the term "regardless of etiology or prognosis," which obviously is uncandid, since if a socially inadequate person is not such by heredity he becomes irrelevant to the legislation proposed. That is, if the social inadequacy is created through some environmental mishap, then certainly the case does not merit any consideration from the standpoint of sterilization.

Note the term "as a useful member of the organized social life of the state." Who shall say who is a useful person? In a capitalistic society a communist can scarcely be declared a useful member of the social life of the state. In a Bolshevik society the capitalist falls at once into the class of the useless. In times of war the pacifist will be defined by all true patriots as worse than useless. In Hitler's Germany, the Jew at one fell swoop is declared as of no value to the state, regardless of the fact that as an Einstein, a Zondek or a Willstätter he may be a brilliant scientist contributing hugely to the welfare of the world. It would be easy to declare that Edgar Allan Poe was a useless member of society, and certainly François Villon, whose name has outlived that of the useful people of his time, was of no special value to the organized state. And so on, and so on. The definition could easily be interpreted against any innovator and against those restless and reckless persons who fail because they attempt too much, but who are the ferment by which the mass is lifted.

"SOCIALLY INADEQUATE" GROUPS

I now come to the crux of the matter—a definition of the socially inadequate classes.

> The socially inadequate classes, *regardless of etiology or prognosis* [italics mine] are the following: (1) feebleminded; (2) insane (including the psychopathic); (3) criminalistic (including the delinquent and wayward); (4) epileptic; (5) inebriate (including drug-habitués); (6) diseased (including the tuberculous, the syphilitic, the leprous, and others with chronic, infectious and legally segregable diseases; (7) blind (including those with seriously impaired hearing); (8) deaf (including those with seriously impaired hearing); (9) deformed (including the crippled); and (10) dependent (including orphans, ne'er-do-wells, the homeless tramps and paupers).

Again I repeat that unless the defects in the groups specified are of hereditary origin their citation in a law of this kind is irrelevant or, if not irrelevant, conceals some purpose which must be challenged at the outset.

I shall consider some of these groups to see in how much, or rather in how little, it is justifiable in the present state of our knowledge to regard them as resulting from the procreative activities of potential parents carrying degenerative qualities.

Feebleminded Group.—This is one of the only two groups which gives any justification whatever to the law under consideration. There

are a few types of feeblemindedness in which familial transmission appears. The world has been flooded, however, with histories of the royal families of feeblemindeddom, such as the Nams, the Jukes, the Kallikaks and the tribes of Ishmael, as if the members of these families were definitely feebleminded, which is not certain, and the families were typical of feebleminded persons in general. The latter inference is entirely incorrect.

In a study which I carried out for the Commonwealth of Massachusetts, which was published in 1930, a survey of the persons confined to institutions, who represent the very worst stock, showed no counterpart of any of those much publicized families. Included in the survey were many families in which feeblemindedness had occurred for two generations and more, but even among these "worst" families there were normal branches producing worth while persons. And for any one of these families there were a dozen in which the feebleminded member was a solitary defective occurring in an otherwise normal familial group not in any way to be distinguished from the rest of the population. Any psychiatrist practicing in a community, who sees the run of people as they are, knows that successful, ordinary and defective parents produce feebleminded offspring.

Popenoe,[2] an ardent advocate of sterilization within proper limits, in studying the social-economic status of the sterilized feebleminded in California, stated:

> The parents of the sterilized patients are distributed within certain limits about the same as the whole male adult population of the state of California *and apparently the greatest number of institutional feebleminded are the children of the skilled laborers, not of the paupers or the casual laboring class* [italics mine]. The same is true of the retarded school children of Munich. . . . While the parentage of the sterilized patients is fairly representative of California as a whole, the small intellectual stratum which produces most of the bright children in the public schools furnishes much less than its quota of mental deficiency.

Continuing in this analysis, Popenoe concluded:

> Since the type of feebleminded requiring institutional care is found to be so widely distributed throughout the whole population, this study supports the view that the selection of any social economic level for sterilization is not an adequate or a scientific procedure. Sterilization must be applied on the merits of each individual case.

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2. For the writings of Paul Popenoe and his group there are many references: Feeblemindedness Today, J. Hered. **21**:421 (Oct.) 1930. Heredity and Behavior, Eugenics **2**:1 (Sept.) 1929. This is an excellent account of criminality. The author stresses heredity but also stresses environment. Heredity and Mental Deficiency, Ment. Hyg. **15**:570 (July) 1931. For a rational sterilization law proposed by Popenoe and his associates of the Human Betterment Foundation, Pasadena, Calif., see the publication of the Human Betterment Foundation entitled "Essential Provisions of Sterilization Laws."

And Tredgold, who is the leading British authority on feeblemindedness and who has published the most cited books, speaking for a distinguished British Commission, stated substantially that if all the feebleminded in the institutions were sterilized and prevented from procreating the effect on the next generation would be minimal so far as the number of feebleminded offspring is concerned.[3]

Jennings substantiated this point of view by stating that the majority of feebleminded persons in each generation descend from the class of "normal" carriers.[4]

The whole program of eugenics in respect to feeblemindedness suffers, first, from an overunification of feeblemindedness, since that condition is not at all sharply differentiated from normalcy, and, second, from the fallacy which Jennings especially attacked, that like produces like through heredity alone. Nothing is further from the truth. Heredity is a mechanism by which the parent transmits like and unlike qualities to his offspring. The whole mendelian hypothesis rests on this fact, and even though mendelianism has become greatly modified, a cardinal principle of the theory is the fact that normal parents, whom no one could by any degree of clairvoyance detect, carry the potentiality of producing feebleminded children.

Insane and Psychopathic Group.—This group has much less right to be regarded as a product of heredity than the feebleminded. In the first place, "insane" is a legal term and has no meaning in science. There are groups of mentally diseased persons in whom the disease has nothing to do with heredity and others in whom the condition seems, at the present writing, to depend on a familial defect. In my own book, "The Inheritance of Mental Diseases," [5] I pointed this out. The difficulty with studies such as those sponsored by the eugenists of Cold Spring Harbor is that a wide variety of conditions are lumped together as one; whole diversities of things are artificially united. Thus, if a father has a sick headache and his descendant has dementia praecox, the two conditions are linked together in a hereditary chain. "All cats look gray in the dark" is an old axiom which applies to most generalizations. Things can be more easily unified by ignorance than by knowledge, since ignorance acts as a common obscuring factor. At any rate, it is completely

3. The British view of the problem is presented in the "Report of the Departmental Committee on Sterilisation" (London, His Majesty's Stationery Office, 1933).

4. For the views of H. S. Jennings, see "The Biological Basis of Human Nature" (New York, W. W. Norton & Company, 1930) and his smaller book, "Prometheus, or Biology and the Advancement of Man (New York, E. P. Dutton & Co., Inc., 1925).

5. Myerson, Abraham: The Inheritance of Mental Diseases, Baltimore, Williams & Wilkins Company, 1925.

passé to speak of the "insane" as if they constituted a class, and when psychopathic persons are included in that class the confusion becomes worse.

Samuel Johnson was a psychopathic person, and so is some shallow sex exhibitionist confined in a county jail. To drink too much is psychopathic, and to drink not at all is also psychopathic. The overgood are psychopathic, as are the oversinful. Lombroso went so far as to state that all geniuses and all defectives are psychopathic, thus linking together under one widespreading canvas the extremes of human mentality. Anybody who is not easily classified can be stigmatized as psychopathic. Except as applied to a few limited groups, the term is used without any real meaning and constitutes one of the darkest places in psychiatry. These difficulties, however, will not be cleared up by any blanket terms which cover ignorance.

The British Departmental Committee on Sterilization came to the conclusion that manic-depressive psychosis is largely hereditary, in support of which they cited the work of Hoffman and Rudin, and that schizophrenia shows an enormous involvement of the descendants. They found practically no other mental diseases that follow hereditary trends in which sterilization would be of any avail. Incidentally, in studying mental defect this distinguished commission stated that my criticism of the work done on the Kallikak family and on other families is destructive and has never been answered.

Furthermore, they stated that environmental factors may be of importance. This point of view has received remarkable confirmation by the work of a group of Chicago sociologists, who, incidentally, have done the best work on feeblemindedness, largely because they used experimental procedures rather than surveys.[6] I cited this work in detail in a recent book.[7] Fundamentally it may be stated that foster children placed early with good families tended to resemble their foster parents more than their real parents in the matter of the intelligence quotient, and that even children born of two feebleminded parents rose above the level of feeblemindedness in the majority of instances if placed out at an early age. It was shown that while heredity operates, which no one will deny, environmental circumstances in the earliest years of life are of enormous importance in raising the level of intelligence. No psychiatrist or neurologist should neglect to read this work carefully. In the same work I also cited other social relationships of intelligence.

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6. Freeman, F. N.; Holzinger, K. J., and Mitchell, B. C.: The Influence of Environment on the Intelligence, School Achievement, and Conduct of Foster Children, Twenty-Seventh Yearbook of the National Society for the Study of Education, Bloomington, Ill., Public School Publishing Company, 1928, p. 103.

7. Myerson, Abraham: Researches in Feeble-Mindedness with Special Relationship to Inheritance, Bull. Massachusetts Dept. Ment. Dis. **14**:108 (April) 1930.

Criminalistic Group Including the Delinquent and Wayward.—The inclusion of this group almost strains one's capacity to be even tolerant. If the "criminalistic," whatever the term may mean, are thus because of heredity, then the proposed law is justified. There is nothing in the literature of crime which indicates this to be so. I refer the reader to the writings of Morris Ploscowe, who has analyzed the literature in the "Report on the Causes of Crime" by the National Commission on Law Observance and Enforcement (George Wickersham, Chairman, June 1931). That analysis shows that criminals are not feebleminded in any greater degree than the rest of the population, even though the most stupid of them are the ones who get caught. It also shows that locality and cultural status play the most important rôle in the genesis of crime, as evidenced by the well known delinquency areas, which play so important a part in modern criminologic literature.

In fact, crime is mainly a matter of social definition. An act which is criminal today may have been legitimate yesterday and may be legitimate again tomorrow, for example, the sale of liquor. It is a crime to be a communist in the United States and a crime to be a capitalist in Russia, as it is a crime to be a Jew in Germany. If one includes in the "criminalistic" group the delinquent and wayward, and especially if one includes those guilty of sex delinquency, then one would have had to impose sterilization on some of the finest figures in the world's history—the greatest poets, the finest painters, the most brilliant writers, the leaders of nations—as well as on every second man and probably on every third woman in the community.

Jennings, who is a true geneticist, has no patience with the talk about eugenic measures in the prevention of crime. He stated:

> It is hard to imagine a more elusive task than the prevention of the formation of those combinations of genes that under certain conditions produce the stupid, the delinquent, and the criminal. If all such persons were prevented from propagation, all conditions remaining the same, this would make very little difference in the number present in the next generation. If the only remedy for criminality is to cut it out of the germ-plasm, as has been asserted, then we shall indeed have the crime wave with us for a long time. . . . Benefit in environmental forces, in treatment of infancy, in education, in tradition, in custom, in ideals, in economic situations, and the organization of society can do much more for these ills of society than can be done through direct attempts to change the genetic constitution of the population.

Epileptic Group.—One can trace the progress made in any branch of medicine, as in the other efforts of man, by the gradually changing character of the discussion in the literature. Once everybody talked about the hereditary character of epilepsy. Today one can read report after report of research without seeing the word heredity mentioned. Lennox and Cobb, who have put forth one of the most recent and one

of the best books on the subject, said a few words about heredity and dismissed that factor by saying that there *may* be an epileptic constitution; but they devoted the rest of their book to studies of the chemical factors underlying the attacks, syphilis, brain pressure, trauma, etc. The use of the concept of constitution is somewhat overworked in medicine. Necessarily, one must have the appropriate constitution to acquire any condition. That is to say, a skull must be made of bone thin enough to be fractured by a falling brick, since a skull made of iron would fracture the brick. It is obviously more important to protect skulls from bricks than to attempt to breed people with thicker or iron skulls. Thus with epilepsy science is now attacking the problem on the very practical and direct bases of the make-up of the brain, the chemical composition of the blood and the interchange of gases and fluids which takes place in the body.

Other Groups.—I might take up in detail each of the other groups listed in the socially inadequate classes, but time and space, as well as patience, forbid. When it comes to the tuberculous and syphilitic and one reflects on the number of able and brilliant persons, not socially inadequate in the least, who are tuberculous and syphilitic and considers that these diseases are infections due to environmental agencies and easily controlled by a determined and humane society, the talk about eugenics becomes intolerable. When to the aforementioned absurdities is added the inclusion of the blind, the deaf, the crippled (which category would include the President of the United States) and the dependent, orphans being clamped together with tramps, the whole thing becomes a mess of incomprehensible bias. Eugenics, like politics, makes strange bedfellows.

THE "CACOGENIC" PERSON

While the foregoing definition of the socially inadequate classes seems like the sheerest and most extravagant of assumptions, there is nothing in the whole history of science to equal the bold jump from the slender spring-board of a few facts into the ocean of claims embodied in the definition of a "cacogenic" person.

> The term "cacogenic" person as herein used is purely a legal expression and shall be applied only to persons declared, under the legal procedure provided by this act, to be potential parents of socially inadequate offspring.

And what is a potential parent of socially inadequate offspring, alias a "cacogenic" person?

> A potential parent of socially inadequate offspring is a person who, regardless of his or her own personal make-up, and of the hereditary nature of such person's co-parent, is a potential parent whose possible offspring, because of the inheritance from said parent of one or more inferior to degenerate physical, physiological, or mental qualities, would, on the average, according to the demonstrated laws of

heredity, most probably function as socially inadequate persons; or whose possible offspring would receive from said parent and would carry in the family-stock but would not necessarily show in the personality, the hereditary basis for one or more inferior or degenerate physical, physiological, or psychological qualities, the appearance of which quality or qualities in the personality would cause the possessor thereof to function as a socially inadequate person, under the normal environment of the state.

The state eugenist, who is to enforce this law by detecting such potential parents, will need to be not a scientist but a clairvoyant. I know of no scientific data or technic by which the "cacogenic" person could be detected, and one can only surmise that the proponents of the "ideal" legislation have in mind some technic of supernatural revelation, some crystal ball or Delphian vision, by which the potentialities of any person's germ plasm in the succeeding generations may be ascertained. There are fine people springing from the most unlikely parents, and the finest parents may bring forth the wildest and most inadequate progeny. True, this is not the rule, but, in fact, there is no demonstrated rule. To mix one's germ plasm with that of another person is to indulge in a game of chance compared to which the faro table is a sober and staid investment. For in the shuffle of the genes which takes place in procreation all the spades may be given to one son or daughter and nothing over a six-spot to his or her brother or sister.

When, however, the definition of a potential parent of socially inadequate offspring is extended to include persons whose progeny do not necessarily show in themselves the inferior qualities but who would transmit them to a third generation, dogmatism becomes an arrogance.

An interesting point made concerning the state eugenist who is to enforce the law is that not only may *he* make the complaint, but it is further provided:

. . . in case of apparent oversight or dereliction by the state eugenicist, any citizen of the state over twenty-one years of age, of sound mind and respected character, may institute proceedings for the legal determination of the question of fact, whether a particular named person is, as such complaining citizen may allege, a potential parent of socially inadequate offspring.

After the complaint of the eugenist or private citizen, the question of fact concerning this highly evolved scientific problem is to be acted on by a judge, or in case of the demand of either party the majority of a jury of six may determine whether or not the *propositus,* as the person accused of being "cacogenic" is labeled, is, in fact, a potential parent of socially inadequate offspring!

Imagine the graft, the blackmail and the generally muddled and corrupt social reactions involved in this proposal! The enforcement of the prohibition law would have been a simple problem, free from corrup-

tion and graft, as compared with the determination as to who is a potential parent of socially inadequate classes. Either the proponents of this legislation are naive beyond my simple powers of expression, or else—what?

The "what" appears revealed in an editorial which appeared in the *Eugenical News*.[8] The *Eugenical News* is the organ of the Galton Society of the International Federation of Eugenic Organizations and of the Third International Congress of Eugenics; its editors are such notables as C. B. Davenport, H. H. Laughlin and Morris Steggerda. The editorial in question is entitled "Race Integrity," and it starts out with this statement:

> The principle of race integrity implies the right of every race to maintain its racial purity and to set ideals for its own physical, mental and spiritual constitution, towards the attainment of which, by migration control and selective breeding, the particular race strives. Within its own territory each race must, by all humanity, be granted the right to promote its own race integrity. The right to strive for race integrity is like the pursuit of happiness; it is one of those things which is not given by one human group to another, but it is an inherent right. *An alien in a host country exists there either by virtue of his military prowess—a conqueror, or on sufferance of the host country, and not in accordance with any inherent rights either moral or legal. Inherent rights are enjoyed by races only in their home countries* [italics mine]. . .
>
> It is the business of eugenics, both as a pure and as an applied science in each country, to collaborate with its national leadership in establishing the racial and family-stock ideals for the particular country, and in striving for the attainment of the established ideals.

This is a denial of all the principles established by modern civilization and a direct reversion backward to the time when the stranger had no rights whatever. It thus establishes as legal and proper the principle of sterilization of aliens in any land and substantiates the right, for example, of Hitler's Germany to cut the vas deferens and fallopian tubes of the Jews of that country. Provided the Nordic inhabitants of the United States rose in their majority and seized the power, they could decree by whatever means the nonpropagation of Italians, Jews and Negroes.

A further editorial note appearing in the *Eugenical News*[9] confirms this criticism:

> Without race dominance, and paradoxical as it may seem, without race pride, practical eugenics cannot be very successful. It is the business of each race and family to take stock of its own qualities, to establish its own ideals, and to breed towards such ideals.

This note is the quintessence of contradiction. In the first place, certainly each family cannot establish its own ideals and breed toward

8. Race Integrity, Eugenical News **18**:77 (July-Aug.) 1933.
9. Eugenical News **17**:112 (Sept.-Oct.) 1932.

such ideals. The family classified as feebleminded, for example, would not be permitted by the sterilization law to breed according to its notions. Nor, if a Nordic movement were successful, could a Semitic family within the confines of a country and in the face of national legislation breed toward its ideals. The apparent fairness of the editorial note is entirely swallowed up by the fact that it contradicts itself and by the fact that racial pride does not coexist with race tolerance.

Logically, any group that becomes dominant in the United States may declare all others alien to the fourth generation and only the persons whose prolific ancestors came over in the remarkably small Mayflower can qualify as members of the American race. This group may establish as their eugenic ideal that only persons of a certain shape, physique and mentality constitute the ideal of the American race, and the infinite variety of other human types, however well qualified they may be to live in some other land, may not correspond to the ideal imposed by the geography and tradition of the United States. The dominant group may go on to declare that persons of the diverse types should be sterilized or prevented from procreating, since apparently sterilization is the chief weapon against the unfit. The Declaration of Independence is thus at once declared to be a noneugenic document of the worst type. It becomes a duty, therefore, both from a scientific and from a social standpoint for neurologists and psychiatrists to attack vigorously and destroy any such eugenic proposals as those here considered before they become translated into the reality of laws which will destroy freedom and individuality.

DISCUSSION

DR. BERNARD SACHS, New York: It is fortunate that this subject has been brought before the members of this association. It is a subject of great public interest, and I think that this association can speak with some authority on the matter and perhaps rid the public of many rather absurd and unproved notions that are gaining vogue. Without attacking the proponents of the law under consideration, I think it would be well following Dr. Myerson's introduction to establish one or two points.

All psychiatrists agree that there is a great deal to be said for the general doctrine of eugenics. As physicians and citizens, they have always been rather careful to advise, so far as possible, that persons in selecting mates keep in mind the character of the family stock and try to marry or have the young people marry into families that are fairly normal physically and mentally. While I endorse the principle, I, like others, have seen some of the eugenic marriages turn out pitifully. And if I were to base the statement on my own personal, individual experience with patients, I should say that I should rather see a random marriage than some of the definitely eugenic marriages that I have known to be contracted, because in several of those eugenic marriages children—not only one child but several children in a generation—have been afflicted with idiocy, with chronic asthma and with other conditions that are regarded as more or less hereditary.

As to the question of eugenics, I think one can simply endorse the doctrine that it is well to be as careful as possible when marriages are entered into and that the question of the health of the offspring should be kept in mind.

As to the question of sterilization, that, I believe, is an entirely different matter because here the principle of heredity with regard to disease enters very definitely into the subject. As to the diseases with which psychiatrists are especially concerned, namely, dementia praecox and manic-depressive psychosis, I think that the question of heredity and, therefore, possibly the question of sterilization may arise.

As regards idiocy and imbecility, so many of the cases are due to accidental occurrences at birth, trauma during labor and so on, that I think the factor of heredity plays less of a rôle in these than it does in many other conditions which particularly interest psychiatrists, especially dementia praecox and manic-depressive psychosis.

Some physicians have been in practice long enough to have seen several generations of families in which these diseases have occurred. I have kept records of some rather prominent groups in which these diseases have occurred, and I am bound to conclude that even in these groups no one would have had the right to practice sterilization. In the three generations in each group, the manic-depressive psychosis had occurred. Yet in the same generations and in each one of the groups, extremely prominent persons have been reared, have led their existence and have been a distinct advantage and an ornament to society. In several of the families some members of which had a manic-depressive psychosis extraordinarily intelligent and useful citizens have been found.

I question whether one has a right, and whether the state has a right anywhere, in Europe or in this country, to enforce sterilization. Some of our states have evidently gone ahead rather rapidly, and for that reason, as regards future legislation in the United States, I think it is just as well for this association to take a more or less definite stand. Personally, I say that no state has a right or has any sufficient reason to enact sterilization laws. The only situation, it seems to me, in which such sterilization laws would be useful would be if there were great danger of imbeciles and idiots becoming sexually rampant. These persons are, however, so well guarded in asylums and in homes that I think the community really does not run any great risk from them. I therefore believe that psychiatrists should try to impress the public, if possible, with the notion that the question of sterilization, which produces a serious physical mutilation and serious interference with the person's rights and with his method of living, should be considered very carefully in each state. I hold that the whole matter of legislation as regards sterilization has been horribly overdone.

Whether it will be possible to improve the human stock by sterilization laws is an open question. One can afford to take one's chances. Nature, on the whole, is much wiser than any person or individual group, and for that reason I hope that Dr. Myerson's introduction of the subject will be followed by a further expression of sentiment with regard to this matter, namely, that sterilization laws should be extremely well considered, that there is relatively little need for them and that where sterilization is practiced and where it has been more or less indiscriminately recommended more harm than good has been effected.

Dr. Walter Timme, New York: I am exceedingly surprised that in this array of sterilization victims the Eugenic Society forgot to include the large group with inclination to homicide and suicide. I refer to the group affected with the Œdipus, superego and monofixation complexes. I should like to hear Dr. Myerson's reaction to that.

DR. ADOLF MEYER, Baltimore: So far as I can see, there is one essential issue in this program. There has always been a certain amount of danger of prosecution facing the physician who either asks for sterilization or is helpful in the performance of it. About all that one should ask for at present is that a reasonable amount of protection to the physician who performs sterilization according to his best judgment be guaranteed by law.

When it comes to the use of the privilege once granted, there arises the difficult question that Dr. Myerson has, I think, very correctly presented. As a member of the Eugenic Society, I have received documents, which, like many of the productions of eager reform movements, can be extremely embarrassing.

One's friends whose good intentions one would like to support ought to be brought to some realization of the equation of uncertainty that exists in the good wishes which all entertain for progress and improvement.

In legislation, and in so many other things, it is unfortunate that few people are willing to grant the need of individual judgment, individual integrity and individual everything else that cannot be regulated by law, a human matter of much more concern than science seems to be willing to consider. Somehow admiration for science has done a tremendous amount of harm in the direction of minimizing individual responsibility. I am one of the benighted people who still stand for the necessity of concept of individual differences, of individual responsibility, not only when it comes to crime but in any form of socialized and civilized life. Somehow social sciences do not want to have anything to do with the concept. Legislation at the present time is an emotional affair. Thus Dr. Myerson's presentation is really, to me, a reminder of a very broad need, namely, the assertion and specification of responsibility in the attitude of the scientifically minded person when dealing humanly with human problems.

DR. ABRAHAM MYERSON, Boston: Dr. Sachs brought up an interesting point, the difficulty of the eugenic marriage. That reminds me of a story told by Shaw. A beautiful woman wrote him a letter, saying, "You are the wisest man in Europe, and I am the most beautiful woman; let's marry." Shaw replied, "The difficulty might be that the child might inherit my looks and your brains."

Something similar has happened in eugenic marriages. Nobody is wise enough at the present time to encompass even his own heredity scientifically. A eugenic marriage savors of the fantastic overbelief of these times in the pronouncements of "science," and its advocates, therefore, are not critically minded. There is no science of eugenics worth considering so far as the prognostication of the inheritance of any person's qualities may go. Only broad generalities are possible; individual applications are impossible.

Now I think that a limited program of sterilization is appropriate. While there are certain groups that ought to be sterilized from a merely biologic point of view, biology is not the sum total of human life, as has been stressed by Dr. Meyer and Dr. Sachs, and as, I believe, is accepted by every right-minded person at the present time. There is room in the universe for the different people who, though they are psychotic from time to time, contribute something of importance to the world.

If a system of bookkeeping were established and the red and the black of the situation were put down, it might be found that some psychotic persons add valuable contributions to life and that men who could be classified as psychopathic, abnormal, queer and fantastic within a certain sense are a source of a great deal that is worth while in modern culture. A system of bookkeeping has not been inaugurated by the eugenists. They put down only the red, "psychotic," and consequently they propose drastic liquidation measures.

Dr. Timme's question involves two points of view. If one is nonfreudian, as I am, and does not recognize the Œdipus complex, this complex is nonexistent and the eugenic program has nothing to do with it. If one is freudian and believes that the Œdipus complex exists in every human being, as seems to be the case, then eugenics would mean the cutting of one's own throat.

I think that what Dr. Meyer has said sums up the situation. There are situations in life in which one must go very slowly. Everything that comes along labels itself "science." Science is very different from the scientific approach. A man may approach the problem of inheritance of human qualities scientifically, but he, as yet, and mankind, as yet, are unable to be scientific about the subject. A long history of perhaps a hundred years of scientific approach is needed before a science of eugenics can develop. When the science of eugenics appears on the scene, one may legislate. Until that time, eugenics must be mainly research—it ought not to take such concrete form as a drastic sterilization program.

AUTONOMIC RESPONSES TO ELECTRICAL STIMULATION OF HYPOTHALAMUS, PREOPTIC REGION AND SEPTUM

S. W. RANSON, M.D.

H. KABAT, B.S.

AND

H. W. MAGOUN, PH.D.

CHICAGO

Structures lying on the surface of the brain are easily reached and can be stimulated or destroyed without damage to other parts. But difficulty of access has retarded investigation of the functional significance of deeply placed nuclear masses and fiber tracts. To introduce precision into the study of these hidden parts of the brain Horsley and Clarke developed their stereotaxic instrument in 1908.

This instrument consists of a rigid frame which can be firmly fixed to the animal's head by clamps resting on the lower margins of the orbits and plugs in the external auditory meatuses, with bars graduated in millimeters and so arranged that a needle carrier can be brought to any desired point over the brain and the needle then inserted to any desired depth, the position of its point being accurately determined in terms of three rectilinear coordinates with reference to a fixed zero point. For stimulation we use a bipolar needle electrode which is not more than 0.9 mm. in diameter and a faradic current slightly above threshold strength. The details of the technic are given elsewhere.[1]

In cats, under light pentobarbital sodium anesthesia (from 14 to 18 mg. per kilogram), the hypothalamus was explored in the following manner: The electrode was inserted 6 mm. from the midline in some chosen plane, for example 12 mm. in front of the interaural line, and pushed down to a point 3 mm. above the zero horizontal plane. At this point a stimulus was applied. The electrode was then pushed down 1 mm. at a time, with a stimulus at each stop, to a point 5 mm. below zero. The needle was then withdrawn and reinserted in the same frontal plane 1 mm. nearer the midline with stimuli at intervals of 1 mm. as it was pushed down. After this frontal plane had been explored millimeter by millimeter to the midline and 1 mm. beyond, the needle carrier was removed 2 mm. farther caudally and another transverse plane was stimulated millimeter by millimeter in the same manner. This process was carried on row after row (planes 12, 10, 8 and 6). In the following cat the rows of punctures were in planes 13, 11, 9 and 7. In some cats the initial plane of stimulation was as far forward

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1934.

1. Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. (Feestb. C. U. Ariëns Kappers) **38**:534, 1934. Ranson, S. W., and Magoun, H. W.: The Central Path of the Pupilloconstrictor Reflex in Response to Light, Arch. Neurol. & Psychiat. **30**:1193 (Dec.) 1933.

as 23 and in others as far back as 7. In this way the hypothalamus and the surrounding territory were systematically explored by stimulating in orderly succession every cubic millimeter of their substance. A record was kept of the coordinates of each point stimulated and the nature of the response. The brains were prepared for microscopic study, and the location of each point stimulated was determined from a study of the sections.

The tracings were made on a long paper kymograph. Pressure within the partly filled bladder was recorded by a tambour, and respiration was recorded by another tambour connected with a tracheal cannula. The blood pressure was recorded through a mercury manometer from the carotid artery.

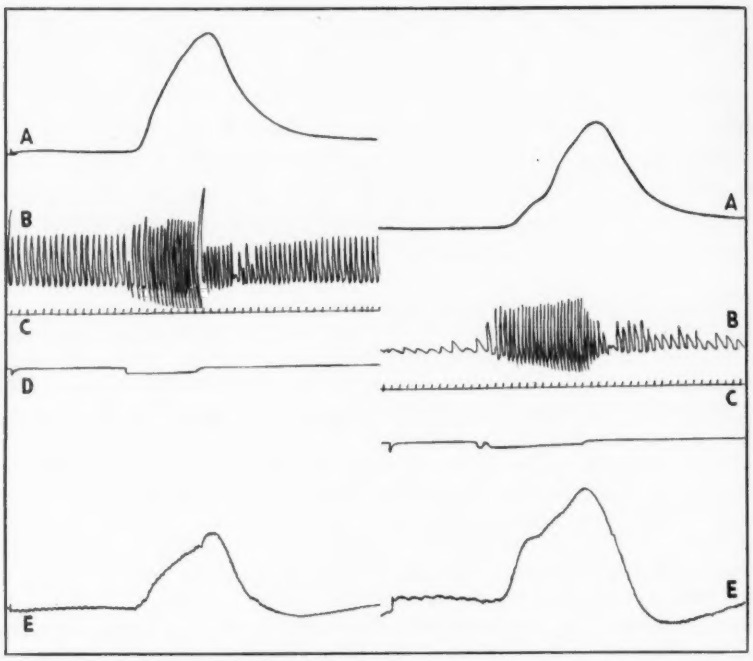

Fig. 1.—Kymographic tracings showing at *A* an increase in intravesical pressure (contraction of the bladder), at *B* an increase in the rate and depth of respiration and at *E* a rise in blood pressure resulting from stimulation of the hypothalamus. *C* indicates the time in seconds, and *D*, the signal. The points yielding these two tracings were symmetrically placed, one on the right and the other on the left side, in the lateral hypothalamic nucleus among the fibers of the medial bundle of the forebrain dorsolateral to the fornix and midway between the latter and the mamillothalamic tract.

RESULTS

Stimulation of the hypothalamus causes a rise in blood pressure, acceleration and increased depth of respiration and contraction of the bladder (fig. 1). These responses are regularly associated with dilatation of the pupils. They are obtained easily and regularly.

Dilatation of the pupils and contraction of the blood vessels are responses mediated through the sympathetic system and are regularly associated with an increased rate and depth of respiration during hypothalamic stimulation. The responses occur in similar association during intense emotional excitement. Contraction of the bladder is a parasympathetic response mediated through the visceral branches of the sacral nerves.

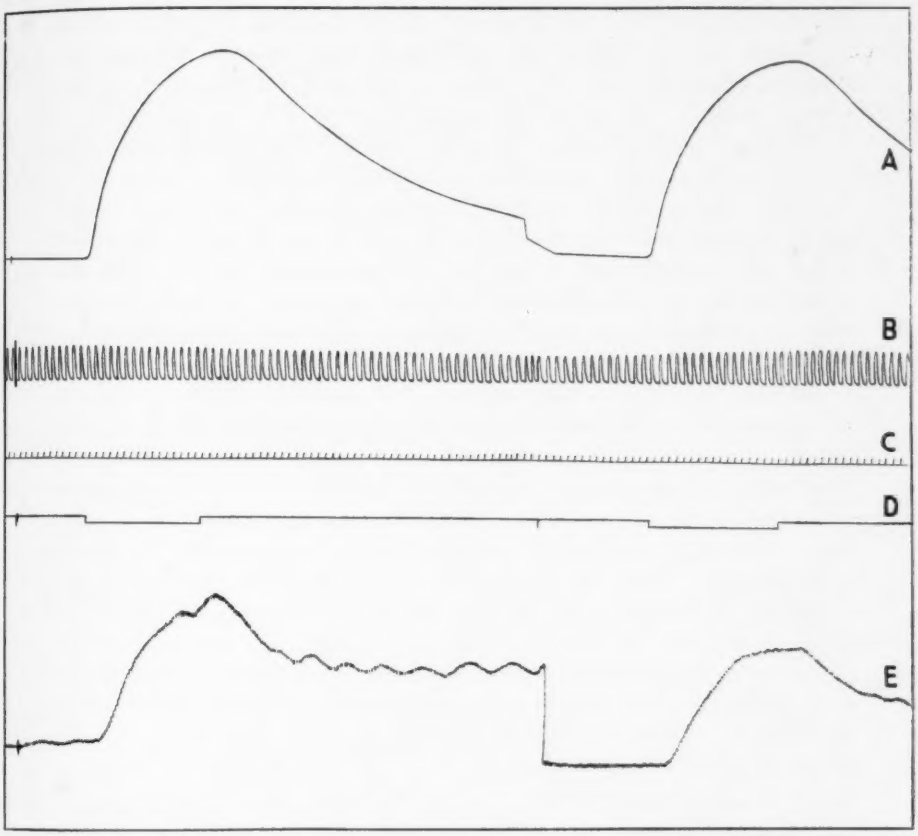

Fig. 2.—Kymographic tracings showing at *A* an increase in intravesical pressure (contraction of the bladder) and at *E* a rise in blood pressure resulting from hypothalamic stimulation in a curarized cat. *B* indicates artificial respiration; *C*, the time in seconds, and *D*, the signal. The record represents the effects of two successive stimulations of one point in almost identically the same position as the points yielding the responses shown in figure 1, but for the record shown in figure 2 the point was a little more ventrally placed, being situated laterally instead of dorsolaterally to the fornix.

Some seconds after the appearance of these autonomic and respiratory reactions the excitation caused by continued stimulation of the

hypothalamus sometimes overflows into somatic paths. Running movements and even struggling may occur, but it is clear from the tracings that somatic contractions are not responsible for the rise in blood pressure or for the increased pressure within the bladder, because the autonomic responses appear first and because they are represented in the kymographic records by smooth curves. But to establish this point beyond dispute the experiments were repeated with curare.

We were fortunate in obtaining a good preparation of curare which completely abolished respiration and all other somatic activity without producing any permanent fall in blood pressure. It was administered intravenously in 0.5 per cent solution, the injection being made slowly over a period of ten or fifteen minutes; about 4 cc. was required to produce the desired effect. Under artificial respiration and while somatic activity was completely abolished, stimulation of the hypothalamus caused rises in blood pressure and contractions of the bladder which were just as marked as those obtained from the same cats before curare was administered or from other normal cats (fig. 2). The rise in arterial and intravesical pressure, therefore, cannot be caused by contraction of skeletal muscles but represent true visceral reactions.

While these responses are sometimes obtained from near the ventricular wall, they are more easily and regularly obtained from the lateral part of the hypothalamus in the region occupied by the medial bundle of the forebrain even up to the edge of the internal capsule. They can also be obtained around the fornix but are not related to either the internal capsule or the fornix because they cannot be obtained from these structures except where they border on or lie within the hypothalamus. These reactions cannot be obtained from the overlying thalamus. Throughout the anteroposterior length of the hypothalamus they can best be obtained from its lateral part. At the level of the mamillary body the reactive zone is that occupied by the medial bundle of the forebrain dorsolateral to the mamillary nuclei. From this point the reactive column can be traced back into the tegmentum of the mesencephalon. Good responses were quite regularly obtained also from points dorsal to the mamillary nuclei in the supramamillary decussation. At this level the reactions can be obtained close to the midline along a narrow zone extending from the supramamillary decussation backward into the central gray matter as well as from the region dorsolateral to the mamillary nuclei. It seems probable that fibers descending from the hypothalamus into the brain stem undergo a partial crossing in the supramamillary decussation and that some of them then descend in the tegmentum of the mesencephalon and others in the central gray matter.

Karplus and Kreidl [2] were correct in saying that sympathetic responses can be obtained from the neighborhood of the subthalamic

2. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: Ein Sympathicuszentrum im Zwischenhirn, Arch. f. d. ges. Physiol. **135**:401, 1910.

nucleus of Luys. They have frequently been misquoted as saying that this nucleus is the hypothalamic sympathetic center. Our results show clearly that this nucleus is not concerned with pupillary dilatation, increases in blood pressure or contraction of the bladder. But these responses are elicited most easily and typically from the region lying on the medial side of this nucleus in the lateral part of the hypothalamus.

The hypothalamic sympathetic center extends forward as far as the optic chiasm but cannot be traced forward beyond that point. At levels rostral to the chiasm and farther forward the medial bundle of the forebrain can be stimulated without yielding any sympathetic responses, showing that the fibers of this bundle, which run backward into the

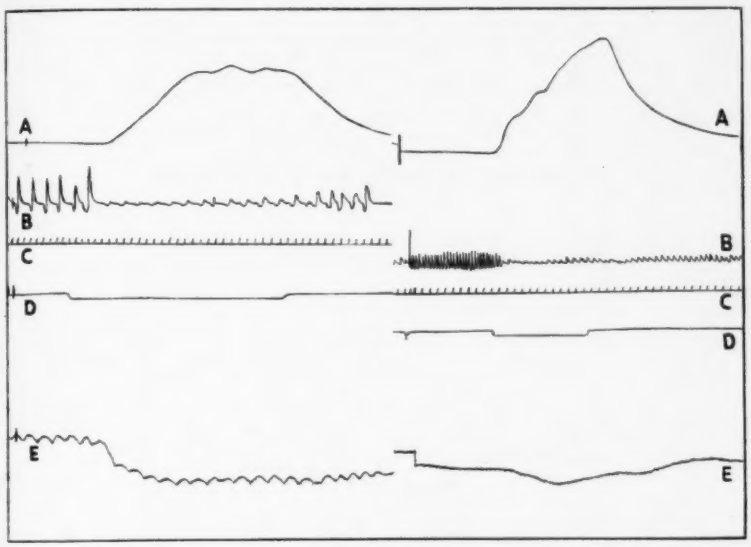

Fig. 3.—Kymographic tracings showing at *A* an increase in intravesical pressure (contraction of the bladder), at *B* a decrease in the rate and depth of respiration and at *E* a fall in blood pressure resulting from stimulation of the septum just rostral to the anterior commissure. *C* indicates the time in seconds, and *D*, the signal.

hypothalamus from more rostrally situated olfactory centers, are not responsible for the reaction. Unlike the sympathetic reactions such as dilatation of the pupils and contraction of the blood vessels, the parasympathetic response of the bladder can be traced forward through the medial part of the preoptic area to the region of the anterior commissure.

Good contractions of the bladder associated with a decrease in the rate and depth of respiration and sometimes with a fall in blood pressure (fig. 3) are obtained from the region immediately in front of the hypothalamus, i. e., from the region surrounding the anterior com-

missure. The same type of reaction is obtained from the septum just in front of the anterior commissure. Contraction of the bladder is obtained with great regularity from the region of the anterior commissure and from the adjacent portion of the septum but cannot be traced forward beyond that point; we believe that nuclear masses concerned in this reaction are located at that point and that a conduction pathway arising here passes back through the hypothalamus in close relation to the hypothalamic sympathetic centers. That is to say, a parasympathetic center for the bladder seems to be located just in front of the hypothalamus in the preoptic region.

There is the sharpest possible contrast between the respiratory reactions obtained from the preoptic region and septum on the one hand

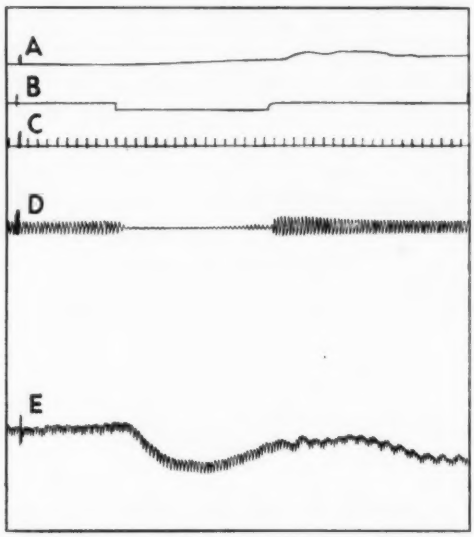

Fig. 4.—Kymographic record showing at *D* a decrease in the rate and depth of respiration and at *E* a drop in blood pressure and a slowing of the heart beat resulting from stimulation of the preoptic area between the medial bundle of the forebrain and the rostral border of the anterior commissure. *A* indicates the reaction of the bladder, *B*, the signal, and *C*, the time in seconds.

and those obtained from the hypothalamus on the other. Stimulation of points in front of the optic chiasm causes the breathing to become slow and shallow (fig. 3) while the same stimulus applied behind the chiasm increases the rate and depth of respiration (fig. 1).

While rises in blood pressure are never obtained from the region of the anterior commissure and adjacent portion of the septum, drops in blood pressure sometimes are (fig. 3), but not with any great regularity. Occasionally we have obtained from stimulation of this region a good depressor reaction with a definite slowing of the pulse indicating

an inhibition of the heart beat through the vagus nerve (fig. 4). This suggests the possibility that one is dealing here with a general parasympathetic center. While this is possible, we are still doubtful as to the existence of such a general parasympathetic center comparable to the sympathetic center in the hypothalamus. More evidence that the vagus nerve can be activated from this region needs to be obtained.

It has long been known that stimulation of the hypothalamus causes pupillary dilatation,[3] an increase in blood pressure,[4] and contraction of the bladder.[5] The negative results observed by Leiter and Grinker[6] are to be attributed to an unsatisfactory technic. The suggestion has been made that the parasympathetic and sympathetic divisions of the autonomic system are separately represented in the hypothalamus.[7] Our evidence does not support the view held by Beattie[8] that the tuber cinereum has parasympathetic functions. According to our findings, sympathetic reactions can be obtained not only from the posterior but from the anterior part of the hypothalamus as far forward as the optic chiasm. The only parasympathetic reaction regularly observed was contraction of the bladder, and the center for this reaction seems to be located in front of the optic chiasm.

We have no evidence that the supra-optic or tangential nucleus is included in this sympathetic center, and that nucleus does not appear to be concerned with contraction of the bladder. It is well established that the supra-optic or tangential nucleus is connected with the posterior lobe of the hypophysis by the tractus hypothalamicohypophyseus, and the two appear to be in close functional association.

In the experiments which have just been described and which were conducted on animals under light pentobarbital sodium anesthesia, dilatation of the pupils and rise in blood pressure were the two sympathetic responses commonly observed. Salivation, sweating and erection of hair were rarely seen. No peristalsis could be observed in the stomach or

3. Ranson, S. W., and Magoun, H. W.: Respiratory and Pupillary Reactions Induced by Electrical Stimulation of the Hypothalamus, Arch. Neurol. & Psychiat. **29**:1179 (June) 1933. Karplus and Kreidl.[2]

4. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: Ueber Beziehungen der Hypothalamuszentren zu Blutdruck und innerer Sekretion, Arch. f. d. ges. Physiol. **215**:667, 1927.

5. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus: Zwischenhirnbasis und Halssympathicus, Arch. f. d. ges. Physiol. **129**:138, 1909.

6. Leiter, L., and Grinker, R. R.: Rôle of the Hypothalamus in Regulation of Blood Pressure: Experimental Studies, with Observations on Respiration, Arch. Neurol. & Psychiat. **31**:54 (Jan.) 1934.

7. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic System, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

8. Beattie, J.: The Relation of the Tuber Cinereum to Gastric and Cardiac Functions, Canad. M. A. J. **26**:278, 1932. Beattie, J. H., and Sheenan, D.: The Effects of Hypothalamic Stimulation on Gastric Motility, J. Physiol. **81**:218, 1934.

intestine either during stimulation or in the intervals between the applications of stimuli. Although this absence of gastro-intestinal motility may be explained by the fact that the animals had had no food for eighteen hours, it was necessary to take into consideration the possibility that parasympathetic reactions may have been suppressed by the anesthetic.

In order to do away with the necessity of an anesthetic the tip of a bipolar needle-like electrode was inserted into the hypothalamus with the apparatus of Horsley and Clarke, and the electrode was then cemented in place so that it was immovably fixed to the skull. This was done under ether anesthesia, and time was then allowed for recovery from the anesthetic. In waking animals stimulation of the hypothalamus with a faradic current slightly above threshold strength produces a picture of intense emotional excitement. If the stimulus is applied when the animal is lying quietly with the eyes closed, the eyes open at once and the pupils are seen to be fully dilated. The respirations become deep and rapid. Shortly after the stimulus is applied the hair on the back and tail becomes fully erected. The excitation spreads so as to include the skeletal as well as the visceral musculature. The head is raised, and the animal attempts to get on its feet and, being restrained, struggles violently to free itself, clawing and lashing its tail. After the stimulus has been continued for a minute or more, saliva begins to run from the mouth, and small drops of sweat can be seen on the pads of the feet.

Animals prepared in this way have been given meals of barium sulphate and observed under the fluoroscope by Dr. Anson and myself.[9] When peristalsis was seen in the stomach and intestine it could be stopped almost instantly by stimulation of the hypothalamus. As might be expected, inhibition of peristalsis was associated with other signs of sympathetic excitation. In no case has peristalsis been initiated or increased by stimulation.

SUMMARY

Stimulation of the gray matter surrounding the anterior commissure not far from the midline or stimulation of the adjacent portion of the septum inhibits respiration and causes contraction of the bladder and sometimes a drop in the blood pressure. Stimulation of the hypothalamus causes an increase in the rate and depth of respiration, an increase in the blood pressure, inhibition of gastro-intestinal peristalsis and dilatation of the pupils as well as contraction of the bladder.

This brief summary of the reactivity of the hypothalamus will be supplemented in another communication by a detailed analysis of the distribution of the points from which the reactions were obtained.

9. Unpublished data.

DISCUSSION

DR. JOHN F. FULTON, New Haven, Conn.: The report of Dr. Ranson and his co-workers appears important for two reasons: In the first place, the controlled stimulation of discrete parts of the subthalamic region of conscious animals has allowed an anatomic delimitation of the sympathetic centers more accurate, I think, than that achieved by any previous investigator. It is true that Hess succeeded in stimulating this area in animals, but his results have certainly given less satisfactory information from the point of view of localization than those of Ranson and his co-workers.

In the second place, I believe that every one will welcome the disclosure that there appears to be no single area of parasympathetic representation. After all, the sympathetic system discharges diffusely, all its parts apparently "going off" at the same time, whereas, the parasympathetic system discharges discretely. When the bladder contracts one does not expect the pupil to constrict, and when the action of the heart is inhibited increased peristalsis does not necessarily occur. The central representation of such a system, discharging appropriately to reflex stimulation through individual channels, must be much more extensive than would be essential for the sympathetic system.

The early work of Barbour indicated that heat regulation was probably governed by the corpus striatum. The recent work of Dr. Spiegel and Dr. Kennard has indicated that extensive autonomic representation, chiefly parasympathetic, exists in the cortex, and I believe that Dr. Ranson's observation that he can obtain movements of the bladder from the anterior commissure and other discrete responses in the autonomic sphere is significant, for it serves to emphasize that parasympathetic representation in the central nervous system is not restricted to a single area and that individual parasympathetic functions are undoubtedly represented at various levels.

I should like to ask Dr. Ranson whether, in harmony with the results of Hess, he has succeeded in inducing signs of sleep by hypothalamic stimulation.

DR. WILDER PENFIELD, Montreal, Canada: It is a great pleasure to hear this presentation which Dr. Ranson has called an orderly exploration of a region in which all neurologists are much interested. It seems to me, a priori, that there is no reason to expect a discrete and exclusive representation of the sympathetic and parasympathetic system. His demonstration therefore seems more reasonable than the work of some earlier workers. The final common pathways of these systems may be separate, but that does not imply that cortical representation should be thus separated.

There are one or two questions I should like to ask. In stimulating the cortex, certainly in stimulating the cortex of a conscious human being when there is no question of anesthesia, one gets different results from stimulation of the same area in different patients. Also, if one produces a movement of a certain part of the body there is often evidence of facilitation for that movement, so that the movement reappears as the result of the stimulation at a distance in an area in which anatomically one would not expect that movement. This is true particularly in epileptic subjects, in whom the same movement may be elicited from areas 6 or 7 cm. distant on the cortex. There are marked evidences of inhibition as well as of facilitation in the human cortex. I should like to ask Dr. Ranson what evidence of migration of function he encountered in the diencephalon.

The procedure of passing a needle in millimeter squares one stab after another is open, it seems to me, to criticism, as after a certain number of stabs have been

made edema and some effect on the adjacent regions of the brain must result. Does not the final stab therefore give less accurate information than the first? The problem is one in which all neurophysiologists are interested at the moment, and Dr. Ranson's work marks a welcome advance.

Dr. Foster Kennedy, New York: Dr. Ranson pointed out that stimulation of a certain area uniformly produced contraction of the bladder. It has been generally observed that ordinary incontinence is produced by lesions of the dura in the frontal area, but the localization of this mechanism has never been clear. I had one patient in France in whom a tiny fragment of shell had passed through and through the right frontal lobe. After he recovered from the general effect of the concussion the patient had persistent urinary incontinence. Does Dr. Ranson's work show certain reasons for this or can he explain the relationship of these phenomena?

Dr. Charles Davison, New York: Did Dr. Ranson make any records of the temperature of the animals he observed?

Dr. S. W. Ranson, Chicago: In regard to the question raised by Dr. Fulton, faradic stimulation of the hypothalamus, so far as I know, never produces sleep. All the responses obtained from hypothalamic stimulation are those that accompany emotional excitement: dilatation of the pupil, erection of hair, rise in blood pressure and, after a long latent period, struggling. When the hypothalamus is stimulated in the awakening animal, one obtains the picture of intense emotional excitation, dilated pupils, erect hair on the back and tail, struggling, lashing of the tail, snarling, clawing and biting.

In regard to the improbability of there being a definite parasympathetic center, I may add to Dr. Fulton's statement that my co-workers and I have tried our best, in working with anesthetized and with unanesthetized animals, to get evidences of control of the intestines through the vagus nerve and that we have never succeeded in augmenting the peristalsis in the stomach or intestine from any point in the hypothalamus or preoptic region, although it is exceedingly easy to produce an inhibition of peristalsis.

Dr. Penfield raised the question whether changing conditions affect the response. Of course, the depth of the anesthesia produces an effect, and it is possible to have the animal in bad condition so that no response is obtained, but when a response is obtained from the hypothalamus it is always of the sympathetic type with the admixture of the parasympathetic vesical response. This vesical response is obtained from the hypothalamus and also farther forward. There is not the same sharpness of localization as for the sympathetic responses.

The question of repeated stabs is important. The surgeon regularly inserts into the brain a needle much thicker than the one we use. Our needle is pointed and less than 1 mm. in diameter, so that it produces relatively little damage. There is a fine track of hemorrhage along the line of the needle, and some edema results. In consideration of the facts that we start at the rostral end of the hypothalamus and work back in the direction in which the impulses will follow, so that the preceding punctures do not block the efferent pathway for the effects of stimuli along succeeding punctures and that we allow 2 mm. between the rows of punctures, edema may be ruled out as a source of error in our experiments. In some experiments we have begun the stimulation farther back in the hypothalamus and obtained the same results as if these points had been reached after several rows of punctures had been placed in the more anterior parts of the hypothalamus.

In regard to Dr. Kennedy's question, it seems to me that it is quite possible that in lesions of the frontal lobe this region of the anterior commissure and preoptic region may be stimulated and produce incontinence. In this connection it is interesting that Cobb and Schaltenbrand in examining their decorticated cat stimulated in the region of the septum obtained contraction of the bladder at a point which corresponds closely with the point at which we obtained such a contraction.

In answer to Dr. Davison's question I can only say that although we have taken records of the temperature of the animals we have not obtained any consistent results. Of course, the stimuli we applied have been very brief, and a change in temperature takes time to develop. Our negative results in that respect are not of any particular significance.

SWEATING REACTION IN PATIENTS WITH DISEASES OF THE SPINAL CORD

STUDY OF THE REACTION PRODUCED BY THE INJECTION OF PILOCARPINE HYDROCHLORIDE

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AND
CLARENCE C. HARE, M.D.
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The most convincing evidence of the segmental position of disease of the spinal cord is the objective demonstration of a dermatomic level of sensory loss. When such a demonstration is not possible, pain of segmental distribution, localized atrophy and changes in the reflexes may be the deciding factors in determining the site of the lesion.

The autonomic nervous system has contributed little to the diagnostic localization of morbid processes affecting the spinal cord. This little understood system has mystified rather than aided the clinicians, a fact which doubtless is the logical corollary of the meager knowledge of the physiology of that system. This study is an effort to determine whether the sympathetic system can be made to assist in the localization of disease in the spinal cord. When the usual response to stimulation of the sympathetic system is known, a deviation from that norm may be interpreted as due to a pathologic state. An attempt to use the reaction of the autonomic nervous system to pilocarpine as an aid in localizing lesions of the spinal cord was made by one [1] of us several years ago. The results of that investigation were not encouraging, probably because the majority of the cases investigated were instances of intramedullary disease of the spinal cord; therefore it was decided to continue the investigation and to include cases of extramedullary disease.

A further use of this method of investigation demonstrated the correctness of Langley's [2] interpretation of Horsley's [3] observation that in

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Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 5, 1934.

1. Craig, C. Burns: A Study of the Sweating Reaction Induced by the Administration of Pilocarpine in Diseases of the Spinal Cord, A. Research Nerv. & Ment. Dis., Proc. **9**:569, 1928.

2. Langley, J. N.: The Secretion of Sweat: I. Supposed Inhibitory Nerve Fibres on the Posterior Nerve Roots: Secretion After Denervation, J. Physiol. **56**:110, 1922.

3. Horsley, V.: Diseases of the Vertebral Column and Compression-Paraplegia, in Allbutt, C., and Rolleston, H. D.: System of Medicine, New York, The Macmillan Company, 1910, vol. 7, p. 571.

cases of compression of the spinal cord pilocarpine produces a sharp contrast between the normal and the paralytic areas, the line of junction being marked by drops of sweat. Langley pointed out that the procedure involved two factors: (1) the stimulation of normal sweating by warming the patient with blankets and (2) the augmentation of this sweating by the administration of pilocarpine. The first reaction is the result of central action, the sweating being brought about by the action of the heat-controlling medullary center; the second phase of the reaction is peripheral and dependent on the stimulating action of pilocarpine on the nerve endings of the glandular effective fibers controlling the activity of the sweat glands.

TECHNIC

The patient was put to bed nude with a sheet and two blankets tucked around him. After half an hour another blanket was added, and ⅕ grain (0.012 Gm.) of pilocarpine hydrochloride was given hypodermically. When the face displayed beads of sweat the patient was uncovered, and the distribution of the sweat over the surface of the body was observed and recorded. The response to the medication was usually rapid, beginning within five minutes and reaching its maximum in twenty or thirty minutes. A segmental location of disease of the spinal cord was considered indicated when the upper part of the body displayed moderate or excessive sweating while the lower part of the body remained dry or comparatively so, the difference in the two zones being definite. As a rule, when a positive level of reaction was present, sweating was excessive over the dermatomes just above the dry area. Lacrimation and salivation were uniformly present, and an urgent desire to urinate was rather frequent.

OBSERVATIONS

The sweating reaction produced by the injection of pilocarpine hydrochloride was tested in thirteen patients with verified extramedullary tumors and in nine patients with intramedullary disease of the spinal cord.

In eleven of thirteen patients with verified extramedullary tumors of the spinal cord the sweating level as elicited by the pilocarpine test corresponded with the segmental location of the tumor as determined at operation. One of the eleven patients had an indefinite sensory level which proved false, and the pilocarpine test revealed a level corresponding with the actual location of the tumor (case 12, table 1). In this case the test was of definite value in localizing the neoplasm and the result corresponded with the site of arrest of iodized poppy-seed oil 40 per cent. In the remaining two patients a sweating level failed to develop.

In contrast, in none of the nine patients with intramedullary disease did a sweating level develop. Patchy areas of sweating or circumferential bands of sweating alternating with bands of comparative dryness which showed no definite level of contrast occurred. This reaction is comparable with the indeterminate demonstrable sensory disorders fre-

TABLE 1.—*Verified Extramedullary Tumors*

Case	Type of Tumor	Subjective Pain	Spinal Block	Compression of the Cord	Sensory Levels*				Segmental Sweating Level After Pilocarpine Hydrochloride*	Vertebral Level of Tumor*	Relation to Cord
					Pain	Temperature	Touch	Vibration			
1	Fibroma	Left shoulder and arm	Doubtful	Absent	C 5	C 5	C 5	Normal	None	C 4 to 6	Left ventral
2	Hemangioblastic fibroblastoma	Right neck and arm	Incomplete	Present	T 1	T 2	T 2	Normal	C 4-T 1 excessive; dry above and below	C 6 to 7	Right dorsal
3	Fibroblastoma	Left arm and digits 4 and 5	Partial	Present	C 4	C 5	C 4	T 10	Right hand dry (C 7 and 8)	C 8 to T 1	Left ventral
4	Hemangioblastoma	Left arm and between shoulders	Slight	Absent	T 4	T 4	T 4	T 4	T 2	C 8 to T 1	Left ventral
5	Fibroblastoma	None	Complete	Present	T 3	T 3	T 3	T 4	T 5	T 1 to 3	Left ventral
6	Fibroblastoma	Both lower extremities	Partial	Present	T 6	T 6	T 6	T 12	T 6	T 4	Left dorsal
7	Fibrochondroma	None	None	Present	T 6	T 6	T 6	T 12	T 5	T 4 to 5	Bilateral ventral (extradural)
8	Fibroblastoma	Girdle at umbilicus	Partial	Present	T 9	T 9	T 9	T 9	T 10	T 8 to 10	Left ventral
9	Hemangioma	Lower thoracic region	Complete	Present	T 7	T 7	T 7	T 7	None	T 8	Bilateral dorsal (extradural)
10	Angiosarcoma	Lumbar region	Partial	Present	T 12	T 12	T 12	Normal	L 1	T 11 to L 1	Bilateral ventral
11	Hemangioblastoma	Lumbar region, right buttock and right leg	Marked	Present	S 1, hyperalgesia	Normal	Normal	Normal	T 12 to L 1	L 2 to 4	Left ventral
12	Fibroma	Lumbar region	None	Absent	C 4 (?)	C 4 (?)	L 4 (?)	Normal	T 12	Conus	Right dorsal
13	Perineurial fibroblastoma	Left sacroiliac region	Marked	Present	S 1	S 1	S 1	Normal	L 1 to 2	Conus and cauda equina	Left anterior

* The letters C, T, L and S designate the cervical, thoracic, lumbar and sacral segments, respectively.

The letters C, T, L and S designate the cervical, thoracic, lumbar and sacral segments, respectively.

TABLE 2.—*Verified Intramedullary Disease of the Spinal Cord*

Case	Diagnosis	Subjective Pain	Spinal Block	Deformity of Cord	Sensory Levels*				Sweating Level After Pilocarpine Hydrochloride*	Vertebral Level Operated*
					Pain	Temperature	Touch	Vibration		
14	Chronic myelitis	Shoulders, arms and legs	None	None	C 3 to 4	C 3 to 4	C 4 to 6	Normal	No level; perspired freely except sacral area which remained dry	C 2 to 5
15	Syringomyelia	Occiput and right shoulder	None	Collapsed	C 3	C 3	C 3	C 8	No level, profuse over right half of body	C 3 to 4
16	Chronic myelitis	Numbness of all extremities and girdle pain	None	Collapsed	Slight diminution in all forms over C 8				No level, profuse on face, scant on chest and below	C 4 to 6
17	Chronic myelitis	Left arm	None	Lateral softening	C 4	C 4	C 4	Normal	Level T 6 on trunk, C 8 on arms	C 4 to 6
18	Intramedullary tumor of cord	Left arm and shoulder	Partial	Spindle-shaped swelling	T 2	T 2	T 2	T 4	Excessive sweating C 6 to 8, dry C 4 to 5	C 5 to 7
19	Chronic lepto-meningitis	Thoracic and lumbar spine	None	Adherent arachnoid	T 12	T 12	T 12	L 2	3 inch (7.62 cm.) band of sweat at T 10, scant above and below	T 5 to 7
20	Chronic myelitis	Lower thorax on coughing	None	Shrunken	T 8	T 12	T 9	T 9	Very slight general sweating reaction to 3/10 grains (0.019 Gm.)	T 8 to 11
21	Meningomyelitis	None	Complete	Swollen	T 11 T 5	T 9 T 4	T 5	L 1	No level, perspired freely except T 9 to L 1	T 9 to 12 and more extensive
22	Varicose veins of cord	Burning in left thigh	None	None	L 1	L 1	L 1	L 1	Sweating above L 2 and dry below	T 10 to 12

* The letters C, T and L designate the cervical, thoracic and lumbar segments, respectively.

quently encountered in patients with intramedullary disease of the spinal cord.

The accompanying tables indicate the clinical data, the sweating reaction to pilocarpine and the location of the tumor or disease of the spinal cord.

The following reports of cases illustrate the entire group. The dotted areas in the figures indicate the regions showing sweating.

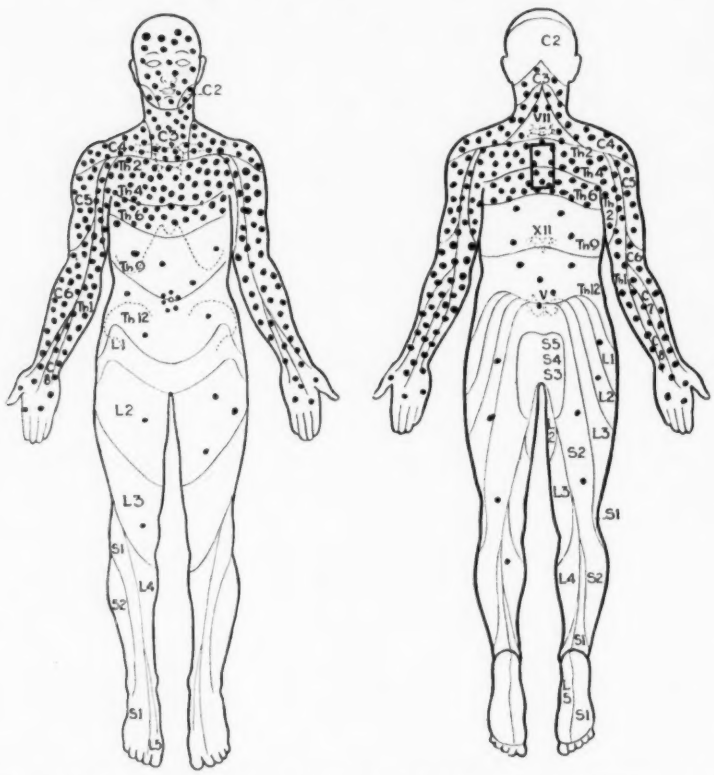

Fig. 1 (case 6).—Sweating level at the sixth thoracic dermatome. A tumor was exposed at the corresponding segment of the spinal cord by laminectomy of the third, fourth and fifth thoracic vertebrae.

REPORT OF CASES

Case 6.—*History.*—A man, aged 62, was admitted to the Neurological Institute of New York on Aug. 24, 1932, complaining of severe sharp pains in both legs, radiating upward to the midthoracic region, of seven months' duration. Walking had become difficult recently because of progressive weakness in the muscles of the legs. Exercise aggravated the radiating pains. For several months the patient had suffered from pain which radiated from the spine around the left side of the midthoracic region.

Examination.—The sensations of touch, pain and temperature were definitely diminished below the level of the sixth thoracic dermatome. Vibratory sensation was lost below the level of the iliac crests. The muscle-joint-tendon sense was intact. The tendon reflexes in the upper extremities were normal; those in the legs, diminished and equal. The abdominal reflexes were absent, and the Babinski sign was present in both feet. Motor power was much diminished in the legs.

Observation.—The injection of ⅓ grain (0.012 Gm.) of pilocarpine hydrochloride revealed a sweating level at the sixth thoracic dermatome (fig. 1). Above that level the skin of the chest, arms, neck and face was profusely covered with large beads of perspiration. Below the sixth thoracic dermatome the skin was only slightly moist. The demarcation was definite between the two areas, showing decidedly different responses. The test was interpreted as indicative of a lesion compressing the spinal cord at a level corresponding to the sixth thoracic dermatome. The manometric test showed a partial subarachnoid block.

Laboratory Data.—The spinal fluid was xanthochromic and contained no cells. The protein content was 720 mg. per hundred cubic centimeters; the reaction for globulin, 4 plus; the Wassermann reaction, negative, and the colloidal gold curve, 111112222.

Operation (Dr. Byron Stookey).—A laminectomy involving the third, fourth and fifth thoracic vertebrae disclosed a subdural ovoid tumor on the left side, dorsolateral to the spinal cord. The tumor was small and soft, and the fifth dorsal nerve root on the left ran diagonally across the middle portion of the mass. The tumor and the nerve root were removed together. Microscopic studies showed the tumor to be a fibroblastoma of the perineural type.

Comment.—This case illustrates the group in which the sensory disorder and the reaction to pilocarpine indicate an identical level of disease in the upper thoracic region of the spinal cord.

CASE 8.—*History.*—A man, aged 53, was admitted to the Neurological Institute of New York on April 25, 1932, complaining of pain in the small of the back, weakness in the left leg and numbness in the left thigh. The pain first appeared in February 1931 in the lower part of the back on the left side, following several hours of skating. It disappeared after a night's rest, only to recur with no apparent cause some weeks later in a more severe form. Subsequently it recurred at irregular intervals. The intervals of freedom from pain became shorter until at the time of admission they were from seven to ten days. The duration of pain varied from hours to days. In June 1931 the patient began to experience attacks of numbness in the left thigh and discovered that the left lower extremity tired more easily than the right. Jerking movements of this extremity in sleep had been observed.

Examination.—The patient displayed a slight limp in the left leg on walking. There was weakness throughout the left lower extremity without atrophy. The reflexes in the upper extremities were less active than the average; those in the lower extremities varied without definite significance. The superficial reflexes were reduced, the left lower abdominal reflexes being persistently absent. Sensory examination revealed anesthesia of diffuse touch and temperature sense and marked hypesthesia to pain below the ninth thoracic dermatome on the left side and the first lumbar dermatome on the right. The muscle-joint sense was lost in the feet and diminished in the knees. Vibration was not perceived in the lower extremities or the pelvis or in the spine up to the ninth thoracic spinous process.

Observation.—Administration of pilocarpine hydrochloride, 1/5 grain (0.012 Gm.) produced profuse perspiration over the head, neck, arms and trunk down to the tenth thoracic dermatome. Below that level the body remained dry (fig. 2). A pilomotor response covered the same area as did the sweating. This result indicated a sharp demarcation due to some pathologic process at the tenth thoracic segment of the spinal cord.

Laboratory Data.—The lumbar spinal fluid was clear and colorless, with 3 cells per cubic millimeter, a 3 plus reaction for globulin and 255 mg. of protein per hundred cubic centimeters; the Wassermann and other tests were negative.

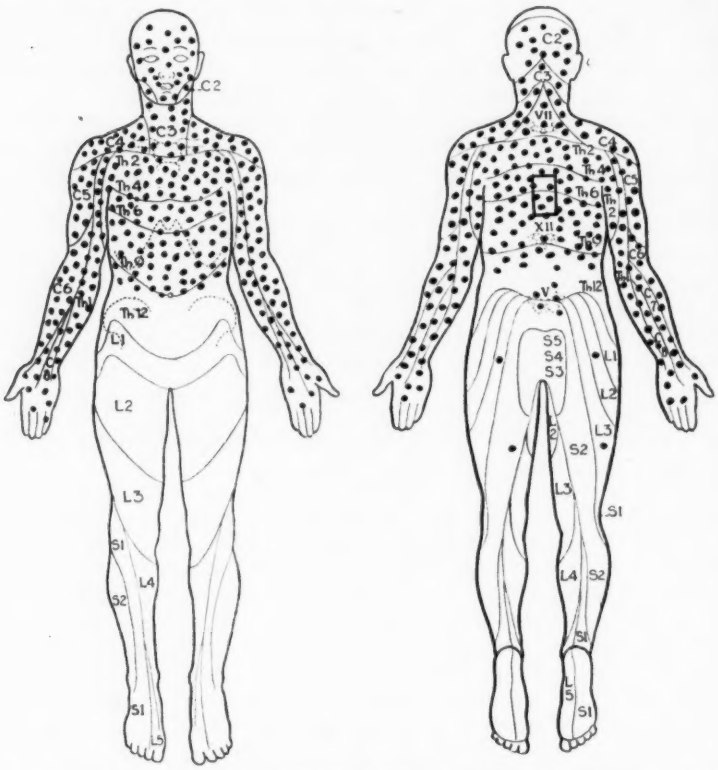

Fig. 2 (case 8).—Sweating level at the tenth thoracic dermatome. A tumor was exposed at the corresponding segment of the spinal cord by laminectomy of the eighth, ninth and tenth thoracic vertebrae.

Operation (Dr. Charles A. Elsberg).—A laminectomy of the eighth, ninth and tenth thoracic vertebrae permitted the removal of a soft extramedullary encapsulated tumor, located ventrally on the left side and adherent to two nerve roots. Histologically the tumor was a fibroblastoma.

Comment.—This case illustrates the group in which the sensory disorders and the reaction to pilocarpine indicate an identical level of disease in the lower thoracic region of the spinal cord.

CASE 11.—*History.*—A truck driver, aged 29, was admitted to the Neurological Institute of New York on Dec. 25, 1932, complaining of severe pain in the lower part of the right side of the back and the right hip and thigh. The course of the illness was intermittent, having begun about a year and a half before the patient came under observation. He was accustomed to lift bags of flour weighing 140 pounds (63.5 Kg.) onto a truck and thought that he might have injured his back in so doing; however, he recalled no particular sprain or accident. Since the first disabling attack in May 1931 he had never been sufficiently free from pain to work, although there were periods of comparative comfort. Coughing and straining increased the pain. He had been in six different hospitals, and the illness

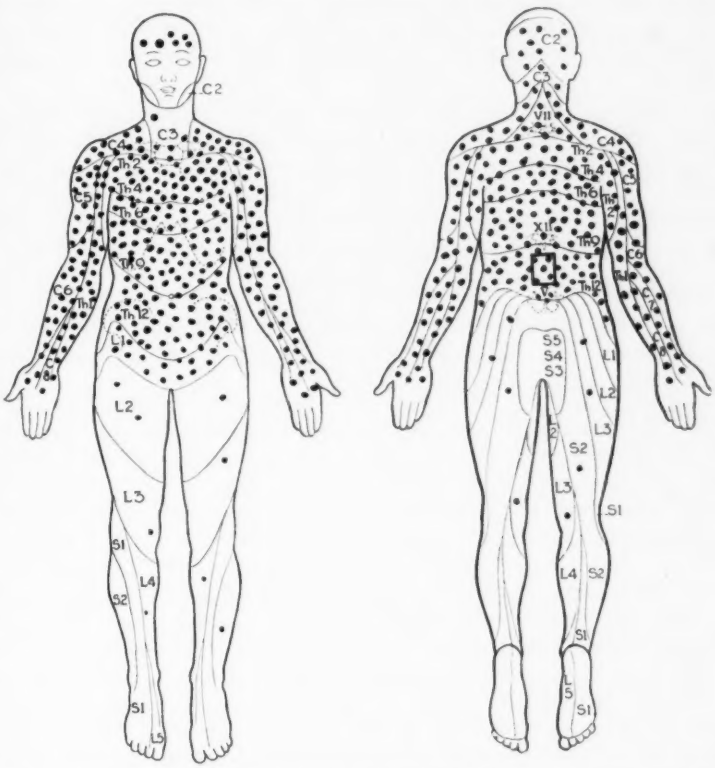

Fig. 3 (case 11).—Sweating level at the twelfth thoracic and first lumbar dermatomes. A tumor was exposed at the segments of the spinal cord just below this level by laminectomy of the second, third and fourth lumbar vertebrae.

had been variously diagnosed as sciatica, sacro-iliac arthritis, neuritis, malingering and addiction to drugs. In the last hospital in which the patient was treated he was given an epidural injection of saline solution in the sacral canal. After two days of relief the pain recurred with increased intensity.

Examination.—The patient was obviously in severe distress and preferred to lie on the left side. He sat down with great caution. In walking the back was held rigidly straight. General and neurologic examinations gave negative results except for the following important findings: The right patellar and suprapatellar tendon reflexes were absent. There were slight atrophy and tenderness of the

right calf and a slight hyperalgesia over the right buttock and inner side of the calf area suggestive of disorder of the second, third and fourth lumbar dermatomes. Diffuse tactile and thermal discriminations were very slightly diminished over the inner surface of the right calf.

Observation.—On Dec. 27, 1932, two days after admission, the injection of pilocarpine hydrochloride, ⅕ grain (0.012 Gm.), resulted in profuse perspiration on the face, neck, arms and trunk down to the groins ventrally and to the first lumbar dermatome dorsally. This reaction suggested compression of the spinal cord at the twelfth thoracic or first lumbar segment (fig. 3).

Laboratory Data.—Spinal fluid obtained from the lumbar sac was xanthochromic, coagulated on standing and showed: cells, 25 per cubic millimeter; reaction for globulin, 4 plus, and protein, 2,000 mg. per hundred cubic centimeters. A manometric test indicated a complete block. All the other tests gave negative results.

Operation (Dr. Earl Brewer).—On Jan. 7, 1933, the laminae of the second, third and fourth lumbar vertebrae were removed, exposing an encapsulated ovoid, plum-colored, cystic tumor lying in the right ventrolateral position and extending the length of the third and fourth lumbar vertebrae and considerably displacing the cauda equina. One large nerve root was adherent to the capsule. Microscopically the tumor was a hemangioblastoma with fibroblastomatous areas.

Comment.—This case illustrates the group in which the sensory disorder, the disorder of the reflexes and the reaction to pilocarpine indicated approximately the same level of disease in the upper lumbar region of the spinal cord.

CASE 12.—*History.*—A man, aged 43, who was admitted to the Neurological Institute of New York on Feb. 5, 1932, complained of difficulty in initiating the urinary flow and pain in the lumbar area radiating down both legs. These symptoms had progressed over a period of two and a half years. One month before admission to the hospital there developed acute urinary retention following a lumbar puncture.

Examination.—The result of the sensory examinations were inconclusive. Different levels of disorder were found by different examiners and at successive examinations by the same examiner. The vibratory and muscle-joint-tendon senses were not altered. There was a constant diminution of tactile sensation over both feet and the lower part of both legs. Tactile sensation was otherwise normal. Several examiners determined the sensory level for painful stimuli to be at the second thoracic dermatome. Other examiners found changes consisting of hyperalgesic zones and considered the level of the lesion to be at either the first thoracic or the first lumbar segment of the cord. Perception of the sensation of heat and cold revealed similar discrepancies. The only alteration of tendon reflexes was a slight exaggeration in the right lower extremity.

Observation.—The pilocarpine test revealed a sweating level at the twelfth thoracic dermatome. Above that level the skin was covered with profuse perspiration, and below it the skin was dry (fig. 4). The results were interpreted as indicating a lesion of the spinal cord at the level of the tenth to the twelfth thoracic segment. A manometric test failed to show a block in the spinal subarachnoid space. Following the injection of iodized poppy-seed oil 40 per cent into the cisterna magna roentgenograms revealed a partial arrest at the level of the first lumbar vertebra.

Laboratory Data.—Spinal fluid from the lumbar subarachnoid space was xanthochromic and showed 10 cells per cubic millimeter, a 3 plus reaction for globulin, 620 mg. of protein per hundred cubic centimeters, a colloidal gold curve of 1111122100 and a negative Wassermann reaction. Fluid from the cisternal space was clear and colorless and contained 25 mg. of protein per hundred cubic centimeters and no cells. Other laboratory data were normal.

Operation (Dr. Charles A. Elsberg).—At operation a large lobulated tumor was found immediately beneath the dura mater extending from the twelfth thoracic to the second lumbar vertebra; it was adherent to and possibly continuous with

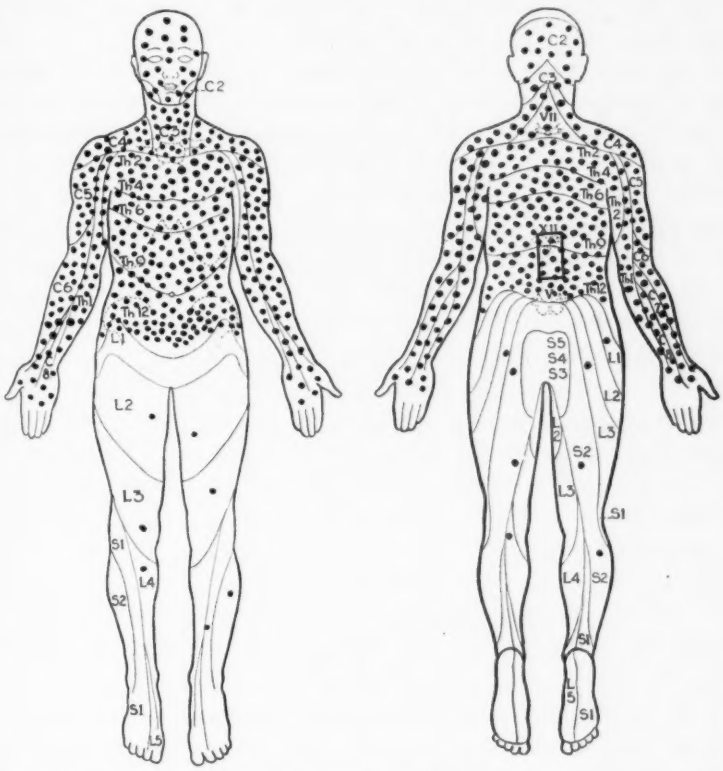

Fig. 4 (case 12).—Sweating level at the twelfth thoracic dermatome. A tumor was exposed at the segments of the spinal cord just below this level by laminectomy of the twelfth thoracic and first and second lumbar vertebrae.

the end of the conus and the upper end of the filum terminale. The mass was soft, was enclosed in a thin capsule and had to be removed in small portions. It proved to be a fibroma.

Comment.—This case illustrates the group in which the sensory disorder is uncertain and of doubtful value in localizing the pathologic disturbance in the spinal cord. Following the administration of pilocar-

pine hydrochloride the sweating level was observed at the junction of the thoracic and lumbar regions of the spinal cord, and this finding was corroborated by the arrest of iodized poppy-seed oil and by operation.

COMMENT

Probably the reaction to pilocarpine is of great value in cases in which a tumor of the spinal cord is suspected but in which a sensory level cannot be determined.

This test may be of value in differentiating intramedullary disease of the spinal cord from extramedullary tumors.

In disease of the spinal cord, if the reaction is diffuse and fails to show definitely differentiated areas of sweating and of lack of it, the probability is that the disease is intramedullary. This is not uniformly true, as in two of the cases of extramedullary tumor a sweating level failed to appear. One may suggest that the failure in one case was due to the fact that the tumor was a hemangioma and therefore probably associated with intramedullary disease. The failure in the other case may have been due to the absence of compression of the cord. Compression of the cord is probably an important factor in causing a differentiated level of sweating in reaction to pilocarpine.

Owing to the comparatively simple arrangement of the thoracic dermatomes it is easier to determine the level of contrasted areas of sweating and of dryness of the skin on the trunk than on the extremities when the cervical, lumbar and sacral dermatomes are involved. This is particularly true when the change from sweating to dryness is gradual and not abrupt.

CONCLUSIONS

Twenty-two verified cases of disease of the spinal cord were studied. The reaction of the sweating mechanism to the injection of pilocarpine hydrochloride was found to be as follows:

1. In cases of intramedullary disease the sweating response rarely shows a level of any diagnostic value. The areas of sweating or of lack of it are scattered irregularly.

2. In cases of extramedullary disease (tumor) the sweating reaction tends to divide the body into contrasting areas, the cephalic area displaying active sweating, the caudal one little or none. The dermatome at the junction of these two areas indicates the segmental location of the tumor. In some cases the dermatomes at the level of the lesion were characterized by unusually excessive sweating.

3. Usually in cases of extramedullary disease the segmental level below which sweating is suppressed corresponds with the level below which sensation is diminished.

DISCUSSION

DR. TEMPLE FAY, Philadelphia: This contribution, in my estimation, adds one more confirmatory sign to the better localization of lesions of the spinal cord and perhaps brings out a means of clinical examination that has not been particularly stressed as a fine point of localization. About seven years ago I called attention to the fact that a vasomotor response could be detected at the upper level of a lesion of the spinal cord in such a way that if the dermatome on the surface of the skin was carefully viewed in reflected light one could map out the vasomotor change that occurred; this vasomotor sign represented the upper root level of the lesion. Now in confirmation of that fact, in twenty-nine verified cases it was seen that while sensory signs were indefinite as to the actual manifestations in the cord and the symptoms of a localized lesion the vasomotor sign proved to be one of the most accurately determining features. This response to sweating and the means by which it may be determined add another important confirmation to the change in vascularity that may result from a lesion irritating and involving the roots of exit. I believe that from a neurologic standpoint this is an important factor. Neurosurgeons in the past have been inclined to explore these lesions with a certain latitude for segmental involvement.

It has been generally believed—Dr. Spiller particularly has emphasized the fact—that from the neurosurgical standpoint the attack on the lesion should be localized on the basis of a lamina rather than on that of an actual segment of the cord. In using the dermatomere on the skin as the highest root of involvement, one is able to determine the lamina, as the root either passes out above in the cervical or below in the thoracic and lumbar spine. By knowing the highest point of involvement of root emergence one is able to determine the operative approach exactly from the standpoint of the lamina. I believe that these signs, that is, the vasomotor sign, the sweating manifestation, the pilomotor manifestation and particularly the Thomas sign (which is induced by compression in the region of the trapezius, producing an ipsilateral pilomotor reflex) are the most valuable adjuncts to localization.

This group of early diagnostic signs seem to me to be far more important than the vague sensory neurologic manifestations which may indicate the presence of a lesion of the cord. I believe that Dr. Craig and Dr. Hare should be congratulated in bringing about more accuracy in this field, because at least in my experience the use of iodized poppy-seed oil has not been required for confirmation. I may say, perhaps to my own embarrassment, that I have used that preparation only once. Dr. Spiller has believed as I do that the localization of a tumor of the spinal cord is a real neurologic art in which there is latitude for deductive sportsmanship. It is like fishing for trout with bait. One may catch the fish by means of mechanical inducement, but it is far more sportsmanlike to use a "dry fly" and match one's wits against the ingenuity of the fish. From a neurologic standpoint, if one can make an accurate localization without mechanical aids it should be done for the sake of the art of neurology if for no other reason. I admit two failures to localize lesions of the cord in my experience. In one case reoperation was performed at a higher level by another neurosurgeon, and again the lesion was not found. In the second case the localization was never reverified. Perhaps the use of iodized poppy-seed oil would have been of benefit in at least one of those cases; nevertheless, I believe that the vasomotor signs offer to neurologists another adjunct to the sportsmanship of the art of neurology and that they improve the accuracy of localization.

DR. BYRON STOOKEY, New York: Several years ago Dr. Klenke and I investigated the sweating reaction in some of the cases of tumors of the spinal cord at the

Neurological Institute. As far as our experience goes, we did not find any levels which were shown by sweating reaction unless there were marked sensory changes. In these extramedullary cases to which Dr. Craig has referred—I believe about thirteen in number—was there not a definite anatomic level as indicated by the sensory findings? In our experience, if sweating reactions occurred, if they showed a level, that level corresponded fairly closely with the sensory level, and the sweating reaction was only a confirmative sign of an already well established level.

I note that Dr. Craig says that he has not been able to establish a level in some of the intrinsic diseases. It seems strange to me from an anatomic standpoint that the sweating reaction should be of diagnostic value. By "being of diagnostic value," I mean being of value when other signs are not present. Of course, if the level is clearcut by the sensory findings the sweating reaction is merely a confirmatory sign and, so far as it is that, it is of great value. But the anatomic supply to the sweat glands of the body is not spread out throughout the entire length of the cord. It is unreasonable to expect that a tumor in the cervical portion of the cord should develop a sweating level. The cervical portion of the cord has no sympathetic outflow to the sweat glands of the body. It begins at about the eighth cervical and fifth thoracic segments, and I do not know whether it has been proved that throughout the whole extent of the cord down to the sacral outflow this whole level of the cord does supply sweating.

Furthermore, it is known from the anatomic pathway of the ganglionic sympathetic fiber that it may enter a sympathetic ganglion of the paravertebral group and terminate immediately after passing through this or in this ganglion. It may make its connection at that point and terminate by postganglionic fiber, or the same preganglionic fiber may enter the sympathetic chain, ascend or descend one, two or three segments and give off a number of collaterals in each sympathetic ganglion. If it does this, it is in the interest of dispersion of its impulse; and with a nervous system which is designed as the sympathetic system is for dispersion and not for localization, I do not believe that one should expect accurate levels to be established either by blushing of the skin or by sweat reaction.

Furthermore, I doubt whether the sympathetic innervation to the sweat glands of the body extends throughout the cord. It is known that certain segments of the cord supply sympathetic preganglionic fibers designed for different functions at different levels; notably, for example, the region from the seventh to the ninth thoracic segments, give a tremendous innervation to the supply of the smooth muscle of the intestine, and all surgeons who have operated on tumors of the spinal cord expect to see tremendous distention after the operation. I think that the precise point (and the locating of that point would, I think, be an interesting experimental study) in the spinal cord in which there is a sympathetic outflow for sweating is yet to be located.

DR. C. BURNS CRAIG, New York: I wish to thank Dr. Fay and Dr. Stookey for their interest in the discussion. Dr. Fay was one of the first to interest himself in and to call attention to autonomic disorders in association with tumors of the cord. The sweating test is a confirmatory test of the sensory level. In only one of these thirteen cases of tumor was it of great value when the determination of the sensory level failed. Many examiners had examined the patient, and they could not agree on the sensory level. The same examiner on different occasions could not establish the same sensory level. The sweating level proved to be the correct one. Sufficient confidence in this test does not exist to warrant an exploration on the basis of the sweating reaction alone; therefore iodized poppy-seed oil was used, and the levels shown by the opaque oil and by the sweating reaction were the same. In most cases the sweating level and the sensory level were approximately

the same. This is not a universal rule. In two of the thirteen cases of tumor no level was obtained. If I stated that the patients with intramedullary disease showed no level, that was an error; two of the nine showed a level.

Dr. Stookey spoke of the effect of the sympathetic nervous system on sweating. Strange to say, the process of sweating is still somewhat of a mystery. Sweating and respiration are the two great avenues for preventing an excessive rise of body temperature. The sympathetic system has little to do with sweating. It is a function of the parasympathetic system. It is closely allied with the activity of the vagus. Just how the parasympathetic fibers work their way to the sweat glands accompanying the sympathetic fibers is not known, but all physiologists concede that sweating is a function of the parasympathetic system.

To me the physiology of this reaction suggests that the parasympathetic system is represented throughout the length of the cord, and I should not be surprised if it is discovered some day that there are cerebral representations—elements of the parasympathetic system extending throughout the axis of the central nervous system.

Dr. John F. Fulton, New Haven, Conn.: Dr. Craig's final comment, that the sweating mechanism may have cerebral representation, is to be taken more seriously than he implied. Perhaps it would be better to refer to the autonomic control of the sweating mechanism, for after the premotor area of the cortex is removed injection of pilocarpine hydrochloride fails to cause normal sweating on the side opposite that of the premotor lesion, and in monkeys in which the cord has been cut injection of this drug fails to cause sweating below the level of transection. The level itself is very sharp, which is scarcely what one would expect if the mechanism were based on a diffuse system of the type described by Dr. Stookey.

EXPERIMENTAL STUDIES IN ALCOHOLISM

I. THE ALCOHOL CONTENT OF THE BLOOD AND CEREBROSPINAL FLUID FOLLOWING ORAL ADMINISTRATION IN CHRONIC ALCOHOLISM AND THE PSYCHOSES

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AND
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Since Nicloux [1] in 1900 first demonstrated that in dogs the blood and cerebrospinal fluid have approximately the same alcohol content, numerous studies have been made on the rise and fall of alcohol concentration in the cerebrospinal fluid following oral ingestion.

In 1930 Abramson and Linde [2] investigated the blood and cerebrospinal fluid relative to their alcohol content after having administered alcohol orally to four patients. No data regarding the drinking habits of the patients were given. The authors concluded that the alcohol concentration of the cerebrospinal fluid rose more slowly than that of the blood and reached its maximum level later, a level which is lower than that of the blood; during the disappearance of the alcohol after the maximum levels have been reached, the alcohol content of the cerebrospinal fluid remains at a higher level than that of the blood.

In 1933 Mehrtens and Newman [3] reviewed the literature and reported experiments in which they administered alcohol intravenously; curves for the alcohol content of the blood and cerebrospinal fluid were made for periods up to eight hours after injection, and the work of Abramson and Linde was confirmed. Cisternal fluid also was obtained in a number of cases and it was found that here the level of the alcohol content rose more promptly and more closely approximated the level in the blood

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From the Boston Psychopathic Hospital.

This paper was read in part at a meeting of the Boston Society of Psychiatry and Neurology, March 15, 1934.

The work was done under the direction of Dr. C. Macfie Campbell, Medical Director, Boston Psychopathic Hospital.

1. Nicloux, M.: Passage de l'alcool ingéré dans quelques liquides de l'organisme, Compt. rend. Soc. de biol. **52**:620 (June) 1900.

2. Abramson, L., and Linde, P.: Zum Uebergang des Aethylalkohols in die Spinalflüssigkeit beim Menschen, Arch. internat. de pharmacodyn. et de thérap. **39**:325, 1930.

3. Mehrtens, H. G., and Newman, H. W.: Alcohol Injected Intravenously: Its Penetration into the Cerebrospinal Fluid in Man, Arch. Neurol. & Psychiat. **30**:1092 (Nov.) 1933.

than does that of the cerebrospinal fluid. When the alcohol content of the blood was kept at a constant level the alcohol concentrations of the cisternal and cerebrospinal fluids after three hours were higher than those of the blood. In a case of subarachnoid block in the upper thoracic region the results indicated a much delayed rise in the level of the alcohol content of the cerebrospinal fluid below the lesion while that of the cisternal fluid was unaffected. The authors concluded that alcohol enters the cerebrospinal fluid by diffusion from the blood, largely via the choroid plexuses. No data regarding the drinking habits of the subjects were given.

It is a matter of common knowledge that the person accustomed to the use of alcohol can drink more and show less toxic symptoms than the person not so accustomed. Although the mechanism of habituation is anything but clear, some light has been thrown on the way in which the organism develops tolerance by the extensive investigations of the past twenty-five years. Pringsheim,[4] working on rats and rabbits, demonstrated that after equivalent doses the alcohol content of the body was higher in nonhabituated animals than in the habituated. He concluded that the latter had acquired the ability to destroy alcohol at a more rapid rate. This was confirmed in man by Schweisheimer,[5] Hansen [6] and Gabbe,[7] who administered alcohol intravenously. Hansen habituated one human subject by giving him 0.5 Gm. of alcohol per kilogram of body weight daily for from three to four weeks. Völtz and Dietrich [8] thought that differences relative to the speed of destruction between habituated and nonhabituated dogs were so slight that no conclusions were justified. Faure and Loewe,[9] in an extensive investigation of alcohol concentrations in the blood in habituated and nonhabituated rabbits, were able to demonstrate that the maximum levels in the blood were higher in the habituated animals and the dropping off from these levels was faster than in the nonhabituated; the higher elevation of maximum levels, they thought, was explained by a more rapid absorption from the gastro-intestinal tract, which was also noted

4. Pringsheim, J.: Chemische Untersuchungen über das Wesen der Alkoholtoleranz, Biochem. Ztschr. **12**:143, 1908.

5. Schweisheimer, L.: Der Alkoholgehalt des Blutes unter verschiedenen Bedingungen, Deutsches Arch. f. klin. Med. **109**:271, 1913.

6. Hansen, K.: Experimentelle Untersuchungen über Gewöhnung an Alkohol beim Menschen, Biochem. Ztschr. **160**:291, 1925.

7. Gabbe, E.: Ueber den Gehalt des Blutes an Alkohol nach intraven. Injektion desselben beim Menschen, Deutsches Arch. f. klin. Med. **122**:81, 1917.

8. Völtz, W., and Dietrich, W.: Ueber die Geschwindigkeit der Alkoholresorption, Biochem. Ztschr. **68**:118, 1915.

9. Faure, W., and Loewe, S.: Der Alkoholspiegel im Blute gewöhnter und ungewöhnter Kaninchen nach einen Probetrunk, Biochem. Ztschr. **143**:47, 1923.

by Völtz and Dietrich in dogs. Graf and Flake [10] have recently investigated the curves for alcohol content of the blood in two persons, one an abstainer, the other habituated over a period of eight weeks with the administration of varying doses of alcohol by mouth. Although they noted marked differences in psychologic reactions, the curves for the blood of the two subjects showed great similarity; they were able to confirm Widmark's [11] observations with regard to the form of the curves, particularly those showing the constant rate of disappearance of alcohol from the blood.

The present investigation is a study of the distribution of orally ingested alcohol in the blood and cerebrospinal fluid of fifty-two subjects especially to determine if differences occur which can be correlated with differences in the clinical picture or in drinking habits.

PROCEDURE

The night before the experiment the subject is weighed and a drink prepared containing 0.6 cc of absolute alcohol per kilogram of body weight, made up in solution so that 100 cc. contains 20 cc. of absolute alcohol and 20 cc. of grape juice. The following morning, with the subject fasting (fourteen hours since the last meal) and lying on the right side, lumbar puncture is performed in the usual aseptic manner, using 2 per cent procaine hydrochloride for local anesthesia. The needle for lumbar puncture is inserted between the third and fourth lumbar vertebrae and left in place during the period of the test (about three hours). A three way turncock is attached so that pressures may be taken and specimens obtained without waste of cerebrospinal fluid. A 2 per cent aqueous solution of mercurochrome is used throughout for sterilization of the skin.

As soon as the needle is in place the pressure of the cerebrospinal fluid is read and the first specimens of fluid and blood are taken. The blood is obtained in the customary manner from one of the superficial veins of the right arm. Then the previously prepared drink, which has been in the refrigerator overnight (tightly stoppered) and is very cold, is administered to the subject who usually drinks it in from one-half to three-fourths minutes. The time is noted as zero minutes and in the course of the following three hours specimens of blood and spinal fluid are taken synchronously at ten, twenty, thirty, forty, fifty, sixty, eighty, one hundred, one hundred and twenty, one hundred and fifty and one hundred and eighty minute intervals. In each instance about 5 cc. of blood and exactly 20 drops of spinal fluid are collected in previously prepared and labeled test tubes, which are then tightly stoppered and kept in the refrigerator at 32 F. until analyzed for alcohol content. The blood is prevented from clotting by the addition of a sufficient amount of potassium oxalate. Just prior to the collection of each sample, 2 drops of cerebrospinal fluid are discarded in order to clear the needle of nonrepresentative fluid.

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10. Graf, O., and Flake, F.: Zur Frage des Verlaufes der Alkoholblutkonzentration nach Alkoholgaben, Arbeitsphysiol. **6**:141, 1932.

11. Widmark, E. M. P.: Les lois cardinales de la distribution et du métabolism de l'alcool ethylique dans l'organisme humain, Lunds Univ. årsskr., 1930, pt. 2, p. 26.

During the experiment the subject lies on the right side, almost immobile, with the legs drawn up, and with only slight changes of position permitted from time to time. He is allowed to read and, if he desires, to smoke during the period of the test. Under these conditions it is surprising how little discomfort the situation seems to cause the average subject.

CHEMICAL METHOD

The method is described for the determination of amounts of alcohol under 100 mg. per hundred cubic centimeters of fluid, but may be extended to smaller or larger ranges. It is based on the principle employed by Nicloux, that of the reduction of potassium bichromate in dilute sulphuric acid, with the subsequent estimation of the excess by ferrous ammonium sulphate and potassium permanganate. The method is modified for the use of the Folin blood filtrate.

Reagents.—The following proportions per liter were used: potassium bichromate, 2.1295 Gm.; ferrous ammonium sulphate, 5.6773 Gm., and potassium permanganate, 0.4577 Gm.

The permanganate is prepared by boiling a solution of it, filtering and titrating against the ferrous ammonium sulphate. The latter retains its strength if kept in a bottle washed with concentrated hydrochloric acid. One cubic centimeter of the bichromate is equivalent to 3 cc. of ferrous ammonium sulphate, 3 cc. of potassium permanganate and 0.5 mg. of alcohol.

The reaction involved in the test is as follows: $3\,C_2H_5OH + 2K_2Cr_2O_7 + 8H_2SO_4 = 3\,CH_3COOH + 2\,K_2SO_4 + 2\,Cr_2(SO_4)_3 + 11\,H_2O$.

Procedure.—Blood: Two cubic centimeters of blood is hemolyzed in 14 cc. of distilled water in a 50 cc. centrifuge tube. Two cubic centimeters of a 10 per cent solution of sodium tungstate is added and the solution shaken. Finally, 2 cc. of two-thirds-normal sulphuric acid is added. The whole is then corked and shaken so that the precipitated protein is consistently distributed throughout the mixture. After standing for five minutes this is centrifugalized for from fifteen to twenty minutes. Ten cubic centimeters of the clear solution is then removed ready for distillation.

Spinal Fluid: One cubic centimeter of spinal fluid is added to 7 cc. of distilled water in a 100 cc. round-bottomed flask; 1 cc. of 10 per cent sodium tungstate and 1 cc. of two-thirds-normal sulphuric acid are added. The mixture is now ready for distillation. The slight precipitation of proteins which occurs prevents excessive foaming.

Distillation and Determination: In each case, 10 cc. of liquid is distilled from a 100 cc. round-bottomed flask through an 8 mm. glass tube about 15 inches (38.1 cm.) long, dipping into a mixture of 5 cc. of eighteen-normal sulphuric acid and 2 cc. of the solution of potassium bichromate contained in a 25 cc. ground glass stoppered mixing cylinder. A microburner is used for the heating, with the flame adjusted so that it requires five minutes to collect 6 cc. of distillate. The receiver is surrounded by a mixture of ice. At the end of five minutes the flask and tube are raised from the flame and the end of the tube is washed with from 1 to 2 cc. of water while the contents of the flask are still boiling. The contents should be close to 15 cc. The stopper of the mixing cylinder is dipped in concentrated sulphuric acid and sealed into the cylinder. The cylinder is placed in a water bath at 85 C. for forty-five minutes, deep enough to cover the level of the liquid. At the end of this time it is removed and cooled. The mixture is now a light yellow color if less than 1 mg. of alcohol was present. A sufficient

even number of cubic centimeters of the ferrous ammonium sulphate is added to give a light green solution without a trace of yellow. The resulting mixture is now titrated with the permanganate to the first appearance of a pink color from a 5 cc. buret graduated into two-hundredth cubic centimeter intervals.

Calculation: The number of milligrams of alcohol per hundred cubic centimeters of blood or cerebrospinal fluid equals:

$$100 \times \frac{\text{cc. } K_2Cr_2O_7 - \frac{\text{cc. Fe} - \text{cc. } KMnO_4}{3}}{2}$$

The method is accurate only if the concentration of acid is close to six-normal; at stronger concentrations the oxidation proceeds partially beyond acetic acid. Additional amounts of oxalate, sulphuric acid or sodium tungstate do not affect the method. Mercurochrome or procaine hydrochloride does not interfere.

There is present in both blood and cerebrospinal fluid a "normal alcohol" content averaging 4 mg. per hundred cubic centimeters. Schweisheimer [5] stated that normal blood contains from 2.9 to 3.6 mg. of alcohol per hundred cubic centimeters. Miles [12] found an average value of 1.7 mg., and Taylor [13] claimed to have shown that this is actually alcohol by standard qualitative tests. Gettler and his co-workers [14] claimed to have isolated it as anhydrous alcohol and found approximately 4 mg. per hundred cubic centimeters of blood. Only Kridelka and Bohet [15] found no volatile reducing substance in blood. This zero error may be in part due to acetone, which gives the same reactions with this method as alcohol.

Accuracy: The error of the method is from 4 to 5 per cent when determining 0.1 mg. of alcohol, and from 1 to 2 per cent with 1 mg. of alcohol.

RESULTS

The experiment was performed on fifty-two subjects: eight with schizophrenia, eight with delirium tremens, nine with alcoholic hallucinosis, nine with syphilis of the central nervous system, two with cerebral arteriosclerosis and one with manic-depressive psychosis (depressed); fifteen of them were without psychosis. According to drinking habits, they were divided into three groups: twenty-five heavy drinkers, fifteen moderate drinkers and twelve abstainers.

The requirements of space prevent the complete tabulation of our detailed results. In cases 2, 13, 18, 27 and 30 more than one experiment was performed; a striking similarity is to be noted between the first and subsequent results in each case. The second experiment in case 13

12. Miles, W. R.: The Comparative Concentrations of Alcohol in Human Blood and Urine at Intervals After Ingestion, J. Pharmacol. & Exper. Therap. **20**:265, 1923.

13. Taylor, A. E.: On the Derivation of Ethyl Alcohol Contained in the Muscle, J. Biol. Chem. **15**:217, 1913.

14. Gettler, Niederl, and Benedetti-Pichler: Isolation of Pure Anhydrous Ethyl Alcohol from Nonalcoholic Human and Animal Tissues, J. Am. Chem. Soc. **54**:1476 (April) 1932.

15. Kridelka, L., and Bohet, M.: Study of the Procedures for the Determination of Ethyl Alcohol in Blood, J. pharm. belgique **11**:413, 1929.

(syphilis of the central nervous system) followed weekly injections of tryparsamide and treatments with diathermy during alternate months. The curves of the two experiments show great similarity, especially when the relationships between the curves for the blood and spinal fluid in each case are considered.

The second experiment in case 18 (syphilis of the central nervous system) followed one month of malarial treatment, while in the third experiment, which followed a month of convalescence, conditions were the same except that twice as much spinal fluid (40 drops) was taken for each specimen. No change is noted in the curves that could be attributed to this change in procedure. The first experiment in case 27 (chronic alcoholism without psychosis) was preceded by several weeks' heavy drinking, while the second experiment followed five months of presumable abstinence, the patient having returned to the hospital for one day in order that the second experiment could be made. No change of significant magnitude is noted between the results of the two experiments. The patient in case 30, a typical case of dementia praecox with auditory hallucinations and gradual withdrawal of interest from the outside world, was the subject of three experiments at intervals of about one month; the curves show a gradual shift from that typical of the abstainer toward that of the heavy drinker (cf. figs. 7, 8 and 9). The cause of this shift is obscure unless the amounts of alcohol given in the first two tests can be considered as habituating doses, which seems improbable. The subject in case 28 received 12 cc. of paraldehyde the night before the experiment and this fact is assumed to be responsible for the high initial values obtained, as paraldehyde would distil and simulate alcohol in the chemical determination used.

It has been possible to form composite curves for the entire group or for any of the subgroups by averaging all the appropriate values for any given time and using the result as the average value for that time. The table records such averages in the several clinical groups as indicated. In the case of total abstainers, moderate drinkers and heavy drinkers the probable error has been computed for each of the averages in these groups as follows: $\frac{0.6745\ \sqrt{Zd^2}}{N}$, when $Z\,d^2$ equals the sum of the squared deviations and N the number of cases; the chances are even in each instance that the true average will fall within the limits of the probable error, and there is practical certainty (9,930 times in 10,000) that it will fall within the limits of $\pm$ 4 times the probable error.[16]

16. Garrett, H. E.: Statistics in Psychology and Education, New York, Longmans, Green and Company, 1926, p. 145.

Average Values of the Alcohol Content of the Blood and Spinal Fluid *

Group	Test	0 Min.		10 Min.		20 Min.		30 Min.		40 Min.		50 Min.		60 Min.		80 Min.		100 Min.		120 Min.		150 Min.		180 Min.	
		Av.	P.E.*	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.	Av.	P.E.
Total abstainers (12 cases)	Blood	3.6	±0.08	24.9	±2.9	41.5	±3.4	55.7	±3.8	61.5	±2.8	62.0	±2.5	60.8	±2.1	55.4	±1.5	50.7	±1.7	46.5	±1.7	42.8	±1.7	34.0	±1.5
	Cerebrospinal fluid	3.6	±0.07	5.6	±0.3	12.5	±1.2	22.3	±2.5	30.6	±3.3	38.8	±3.4	45.0	±3.2	51.5	±2.6	54.2	±2.2	54.6	±1.7	51.9	±1.6	46.5	±1.5
Moderate drinkers (15 cases)	Blood	3.9	±0.09	26.3	±2.2	52.9	±3.1	66.5	±2.6	64.8	±2.2	62.0	±1.7	59.3	±1.5	54.2	±1.2	49.5	±1.1	44.6	±1.1	38.5	±1.2	32.1	±1.4
	Cerebrospinal fluid	3.5	±0.24	6.2	±0.4	10.9	±0.9	17.5	±1.4	26.0	±2.0	33.0	±2.3	39.0	±2.4	45.7	±2.2	49.3	±1.8	50.1	±1.5	49.8	±1.3	46.1	±1.4
Heavy drinkers (25 cases)	Blood	4.2	±0.08	35.6	±2.1	68.5	±2.7	80.2	±1.7	73.3	±1.2	65.2	±1.0	60.5	±0.7	53.7	±0.7	47.4	±0.7	41.6	±0.8	34.8	±0.9	28.4	±1.0
	Cerebrospinal fluid	3.9	±0.08	6.8	±0.3	12.0	±0.5	21.7	±1.1	32.6	±1.5	41.9	±1.8	49.0	±2.0	54.5	±1.7	55.0	±1.2	52.5	±0.9	48.2	±0.9	42.5	±1.1
Syphilis of the central nervous system (9 cases)	Blood	4.1		28.0		55.1		70.6		71.2		67.3		61.9		55.4		50.7		46.1		40.4		32.5	
	Cerebrospinal fluid	3.9		6.6		12.0		20.1		29.0		37.0		42.9		50.1		53.0		53.5		52.0		47.6	
Schizophrenia (8 cases)	Blood	3.9		21.8		39.8		51.4		55.0		56.4		56.6		51.8		47.3		42.6		33.5		31.6	
	Cerebrospinal fluid	3.6		4.9		8.8		13.4		18.4		25.1		31.3		39.7		43.4		45.8		46.9		44.2	
Delirium tremens (8 cases)	Blood	4.3		36.8		63.9		72.9		69.0		64.8		58.8		51.6		45.8		39.6		32.3		24.8	
	Cerebrospinal fluid	4.3		7.0		12.7		23.3		33.3		43.5		50.5		53.9		53.5		50.9		46.1		38.3	
Alcoholic hallucinosis (9 cases)	Blood	4.2		24.3		58.8		76.8		72.4		62.8		58.6		53.7		47.8		42.7		37.5		30.4	
	Cerebrospinal fluid	3.6		5.9		11.0		21.3		32.7		42.2		51.2		58.4		57.1		54.8		50.5		44.9	

* The values are expressed in milligrams per hundred cubic centimeters. Av. indicates the average value in milligrams; P.E., the probable error in per cent.

COMMENT AND CONCLUSIONS

The findings in the group of alcoholic psychoses (figs. 1 and 2) are of interest in that they resemble the average findings for heavy drinkers; no significant or constant difference in values is found between the patients with delirium tremens, those with alcoholic hallucinosis and the nonpsychotic heavy drinkers.

The results in the schizophrenic cases (fig. 3) correspond with those of abstainers in general, which fits in with the fact that six of the eight schizophrenic patients are abstainers, the other two being moderate drinkers.

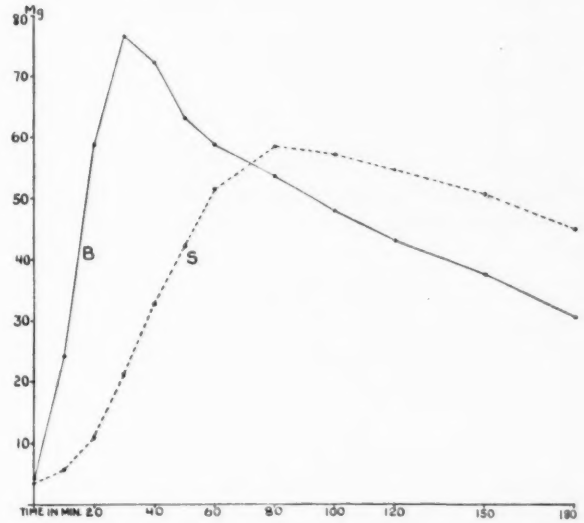

Fig. 1.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) at the time intervals indicated in nine cases of alcoholic hallucinosis. In this and the accompanying figures the quantities are expressed in milligrams per hundred cubic centimeters.

There appear to be no special characteristics brought out by averaging together the values in the cases of syphilis of the central nervous system (fig. 4). The composite curves fall between those for the moderate and heavy drinkers, which agrees with the general drinking habits in the syphilitic group.

The most striking results are obtained when the three general groups —heavy, moderate and nondrinkers—are compared (figs. 5 and 6). It is noted that in heavy drinkers as a group the alcohol content of the blood rises more rapidly, reaches a higher peak and falls more quickly than does that of the abstainers. The moderate drinkers occupy an intermediate position in all three respects. These tendencies can be

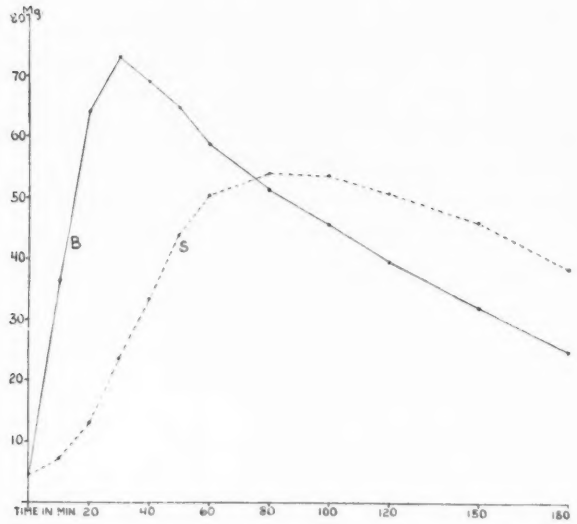

Fig. 2.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in eight cases of delirium tremens.

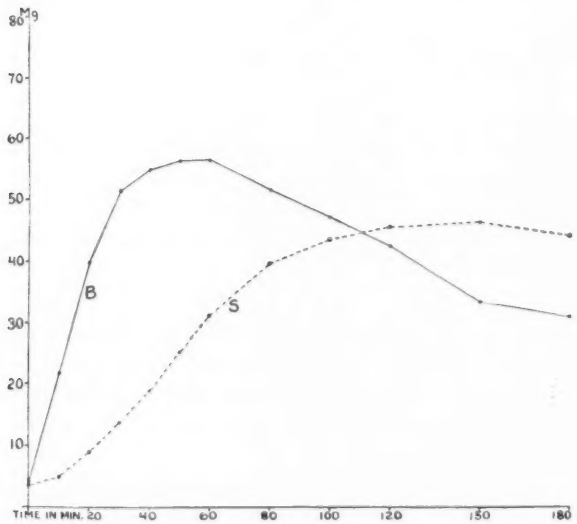

Fig. 3.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in eight cases of schizophrenia.

observed in most of the individual cases as well; although there is considerable variation between any two single curves, the form of each clearly approaches that of the average. The chief difference in the rate of disappearance of the alcohol from the blood seems to occur immediately after the peak has been reached; in the case of heavy drinkers the curve for the alcohol in the blood falls sharply and then later (about one hour) flattens out and runs parallel at a lower level to that of the curves for moderate drinkers and abstainers. This observation on heavy drinkers disagrees with Widmark's[11] finding of a constant rate of disappearance, although such is apparently the case in the groups of moderate drinkers and abstainers. These general findings are in direct contradiction to Schweisheimer's[5] results in the cases of

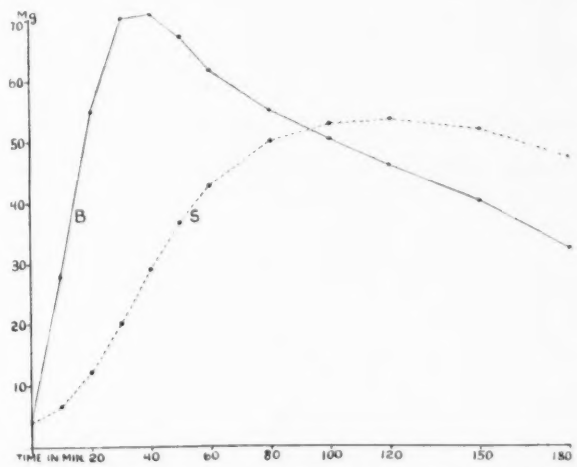

Fig. 4.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in nine cases of syphilis of the central nervous system.

two abstainers, two moderate drinkers and six heavy drinkers. Using oral doses of 1.57 cc. of alcohol per kilogram of body weight, he found that the alcohol content of the blood attained a higher maximum level in abstainers than in heavy drinkers, while Graf and Flake,[10] using two subjects (one habituated, the other a nondrinker) could demonstrate no difference between the two. The present results tend to invalidate earlier conceptions of habituation and indicate the absence of a direct relationship between the alcoholic level of the blood and tolerance, although a correlation between the alcohol content in the blood and drinking habits seems established.

As has been pointed out by earlier investigators,[17] the alcohol curve of the cerebrospinal fluid after oral ingestion rises at a slower rate than that of the blood, and after crossing the curve for the blood maintains

17. Abramson and Linde.[2] Mehrtens and Newman.[3]

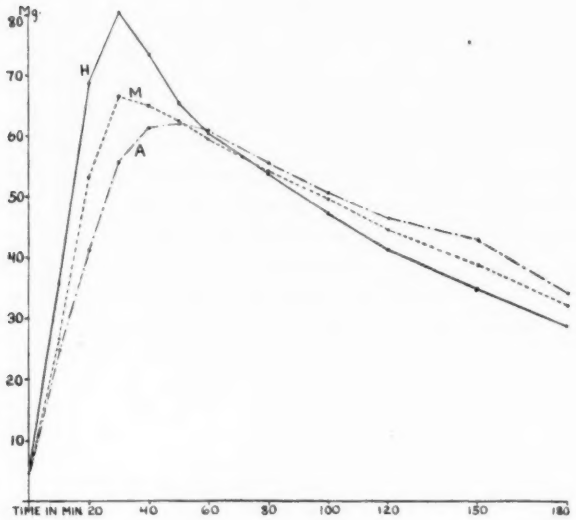

Fig. 5.—Average alcohol content of the blood in the three groups of heavy (*H*) and moderate (*M*) drinkers and abstainers (*A*).

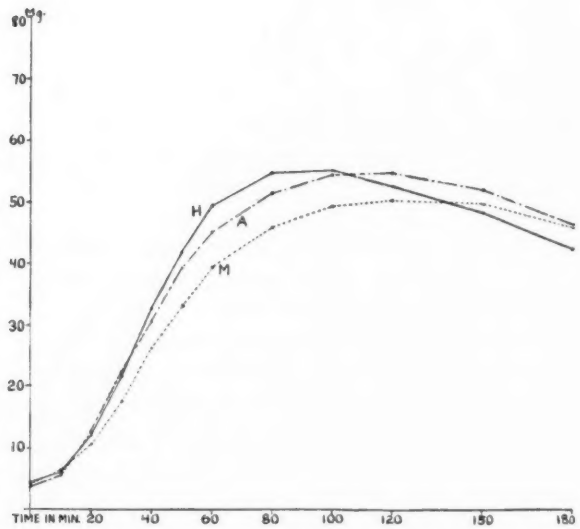

Fig. 6.—Average alcohol content of the spinal fluid in the three groups of heavy (*H*) and moderate (*M*) drinkers and abstainers (*A*).

a higher level. It seems probable that this phenomenon is due, at least partially, to "diffusion lag" between blood and cerebrospinal fluid; that is, the cerebrospinal fluid when formed at the choroid plexuses has essentially the same alcohol concentration at that point as has the blood, but by the time this cerebrospinal fluid has reached the lumbar region extensive changes in alcohol concentration have already occurred in the blood; the cerebrospinal fluid seems to act largely as a metabolically inert reservoir so far as alcohol is concerned (similar to Miles' [12] findings on urinary alcohol in relation to that of the blood). If this is a correct interpretation it seems fair to assume that the differences in the curves for the average alcohol content of cerebrospinal fluid are in the main

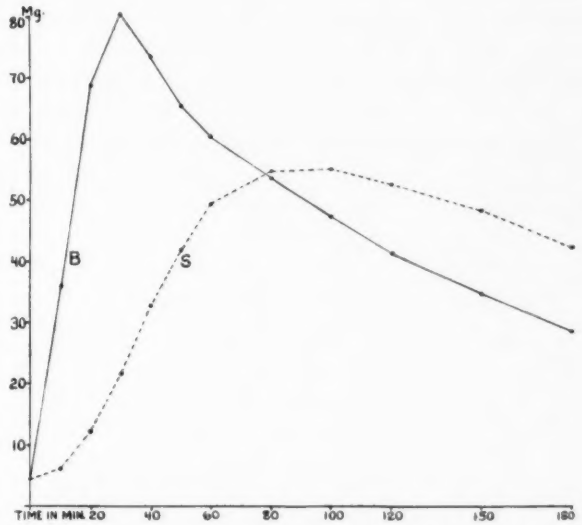

Fig. 7.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in twenty-five heavy drinkers.

secondary to, and dependent on, the differences in those for the blood. It should be noted, however, that the maximum level reached in the cerebrospinal fluid of the moderate drinker is lower in absolute value than in both the other groups, although the maximum level in the blood of the moderate drinker is between the peaks for the heavy and non-drinkers. The meaning of these findings so far as tolerance is concerned is not clear, but they are suggestive of altered relationships in the permeability of the hemato-encephalic barrier in the course of chronic alcoholism. If, as has been suggested by earlier workers,[18]

18. Gettler, A. O., and Freireich, A. W.: Determination of Alcoholic Intoxication During Life by Spinal Fluid Analysis, J. Biol. Chem. **92**:199 (July) 1931. Balthazard, V., and Lambert, M.: Recherches toxicologiques sur l'alcoolisme aigu chez l'homme, Ann. de méd. lég. **1**:83, 1921.

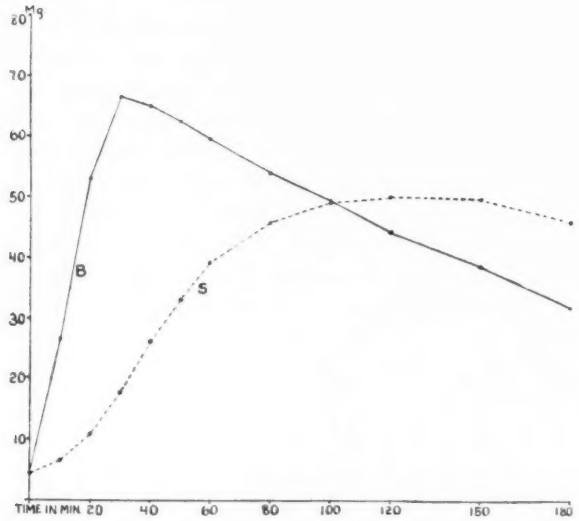

Fig. 8.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in fifteen moderate drinkers.

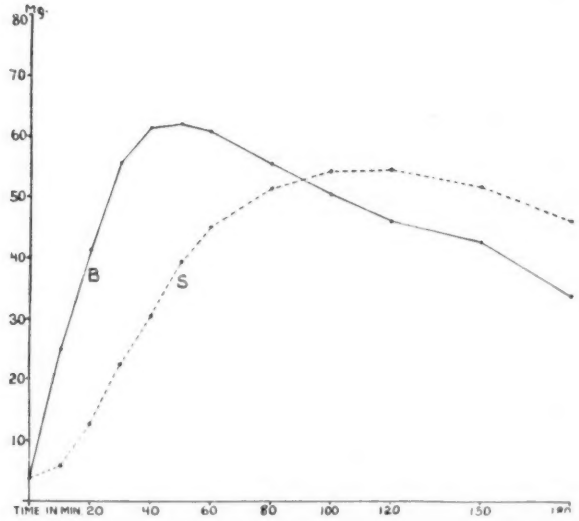

Fig. 9.—Average alcohol content of the blood (*B*) and spinal fluid (*S*) in twelve abstainers.

the alcohol content of the cerebrospinal fluid can be considered representative of the alcohol content of the tissues in general, it would appear that moderate drinkers have acquired the ability to delay the passage of alcohol from the blood into the tissues and, furthermore, that the absolute quantity of alcohol entering the tissues is least in moderate drinkers.

SUMMARY

Curves for synchronous alcohol values of the blood and cerebrospinal fluid covering a period of three hours after the oral administration of 0.6 cc. of absolute alcohol in a 20 per cent solution per kilogram of body weight were constructed in fifty-eight experiments on fifty-two subjects. The chemical method for the determination of the alcohol was based on Nicloux's principle: the reduction of bichromate in dilute sulphuric acid with the subsequent estimation of the excess by ferrous ammonium sulphate and potassium permanganate; the method was modified for use with the Folin blood filtrate.

The experimental subjects consisted of eight patients with schizophrenia, eight with delirium tremens, nine with alcoholic hallucinosis, nine with syphilis of the central nervous system, two with cerebral arteriosclerosis and one with manic-depressive psychosis (depressed); fifteen of the cases were without psychosis. According to drinking habits the subjects were divided into three groups: twenty-five heavy drinkers, fifteen moderate drinkers and twelve abstainers.

Comparison of composite graphs showed important correlations between the type of curves obtained and the drinking habits of the subjects: In heavy drinkers the alcohol of the blood rises more rapidly, reaches a higher maximum and falls more quickly than in abstainers; the values for moderate drinkers occupy an intermediate position. In the cerebrospinal fluid the alcohol rises more rapidly to a higher peak and falls more quickly in the heavy drinkers than in the moderate drinkers, while the curves for the abstainers occupy an intermediate position.

No correlation could be demonstrated between the clinical picture and type of curve: The composite curves for the alcoholic psychoses resembled those for the heavy drinkers and those for the schizophrenic group approached the form in the abstainer group. The general drinking habits of each group seem to determine the shape of the composite curves.

DISCUSSION

DR. C. M. CAMPBELL: The alcoholic psychoses have received scant attention as compared with their social importance. The practical necessities of the situation limit the study of the cases. The acute psychoses of the chronic drinker are familiar—the acute hallucinosis, on the one hand, now apt to be relegated to the schizophrenic group, and on the other hand, delirium tremens and its sequelae. The problem of delirium tremens is largely one for the chemist and the internist.

When the patient becomes addicted to alcohol, it is a problem for the psychiatrist. The intermediate stages of the effect of alcohol on the organism are obviously a problem for the biochemist. It is satisfactory to find one simple stage of the problem being attacked as it has been by Dr. Fleming and Dr. Stotz.

DR. H. H. MERRITT: There is an interesting point in connection with the circulation of the cerebrospinal fluid. Schottmüller and Schumm were the first to find alcohol in the cerebrospinal fluid. They explained it as being due to an affinity of the blood for alcohol. The lag of the amount of alcohol in the spinal fluid as compared with that in the blood is related to the time it takes the fluid to get to the lumbar space from the ventricles. If the curves obtained by Dr. Fleming and Dr. Stotz were put on the board and compared with the curves obtained after the ingestion of dextrose they would be exactly the same. This has also been recently shown very well by Mehrtens. He analyzed cisternal fluid, which is relatively freshly formed, and found that the alcoholic contents of the blood and cerebrospinal fluid ran almost equal.

DR. H. SOLOMON: I wish to learn whether Dr. Fleming and Dr. Stotz found any difference between the heavy drinkers and the abstainers in the schizophrenic group. They showed that the persons with schizophrenia did not have the same increase in the alcoholic content. Is that because they were not heavy drinkers? Do the two groups have similar curves? I think that Dr. Fleming and Dr. Stotz have been carrying on a good many observations regarding the response of patients after the ingestion of alcohol for psychologic purposes.

DR. A. W. STEARNS: I hope that future studies on alcoholism may be viewed with more detachment than they have been in the past. I remember writing a paper which was used by the Brewers' Association to show the benefits obtained from alcohol and by the Antisaloon League to prove it harmful.

DR. R. FLEMING: In regard to Dr. Solomon's question about the differences between the heavy drinkers and the abstainers in the schizophrenic group, our data do not give us much from which to conclude; of the eight persons with schizophrenia, six were abstainers and two were moderate drinkers. In general, the tendencies of the composite curves to vary according to the drinking habits of the subjects can be observed in most of the individual cases as well; although there is considerable variation between any two single curves, the shape of each clearly approaches that of the average.

As far as psychologic effects of alcohol are concerned, Dr. Stotz and I are able to say little at present; the work so far indicates that the blood alcohol level alone does not bear a simple and direct relationship to the psychologic effects; we have noted marked effects at low blood alcohol levels and no demonstrable psychologic effects at high levels. The problem is a complicated one, and probably the answer is not entirely physiologic.

One of our difficulties in interpreting this work has been due to the fact that we were dealing with two variables: the rate at which alcohol passes from the gastro-intestinal tract into the blood, and the rate with which it passes from the blood to the spinal fluid. We are at present engaged in repeating the work with the first variable eliminated by the intravenous administration of alcohol.

PSYCHOLOGY OF A CERTAIN TYPE OF MALINGERING

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In an earlier study [1] of the attenuated forms of suicide, I suggested that self-mutilation, appearing under the varying circumstances of psychosis, neurosis, religious ceremony and social convention, is in all cases the result of a compromise between the self-destructive and erotic tendencies, such that the death instinct is thwarted of its purpose through the sacrifice of a part for the whole.[2] I was able to demonstrate from representative examples of various types of mutilation that in all of them one could find evidence of a simultaneous indulgence in passive gratifications and punitive satisfaction, which at the same time atone for the guilt, repeat the crime (of passivity) and act as a peace-offering for the mitigation of the more severe punishment of death, i. e., a sacrifice to permit continued indulgence.

I did not include in that study a form of self-mutilation with which clinical medicine has been familiar for centuries, namely, malingering. Malingering is a word of obscure origin, of which the earliest known definition appears in Grove's "Directory of the Vulgar Tongue," in which it is defined as "a military term for one who, under pretense of sickness, evades his duty." In the earliest meaning there is some hint as to the dynamic explanation of what would now be called a symptomatic act, which since that time seems to have puzzled and distressed clinicians no end. Although malingering is obviously, in certain forms, a variety of self-mutilation, I was led to a separate consideration of it by reason of two outstanding characteristics which set it apart from the ordinary forms of self-mutilation: first, the large epinosic gain, which is, of course, largely conscious, and, second, the frank appearance of what in every other form of self-mutilation is entirely masked, namely, the aggressive elements.

The first of these differences between malingering and the mutilations carried out by neurotic and psychotic patients is in degree rather than

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1. Menninger, K. A.: Focal Self Destruction, Am. J. Psychiat., to be published.

2. Alexander (Alexander, Franz: The Psychoanalysis of the Total Entity, New York, Nervous & Mental Disease Publishing Company, 1930) called this principle "conscience bribing," and Rado (Rado, S.: Fear of Castration in Women, Psychoanalyt. Quart. **2**:425 [July-Oct.] 1933), the "choice of the lesser evil."

3. This footnote was deleted by the author.

in kind. The malingerer turns his neurotic tendencies to evident profitable account (or attempts to do so) and takes conscious cognizance of this. In psychoanalytic language, he consciously capitalizes the secondary gain of illness and makes it the predominant motive.[4]

In doing so, however, he necessarily thwarts the physician and other people whose interests run counter to his, and in this way he carries out aggressions toward a substitute object. Usually in the end the object is the physician; and because he is the victim of an unjustified aggression, the physician's temptation to retaliate may result in making the patient suffer doubly.

This becomes clear if one reads in a detached and impassive way almost any account of malingering in the medical literature. What impresses one most is the apparent irritation, hostility, even righteous indignation of the authors toward the subjects of their investigations.

In their comprehensive monograph on the subject, for example, Jones and Llewellyn[5] returned time after time to the moral obliquity of the malingerer, his knavery, his rascality, his unscrupulousness. Many pages of their book, as well as many of the articles that appear in medical literature, are devoted to the technic of distinguishing between

4. Every neurotic patient makes some use of this secondary gain from illness, as is well known, and to this extent every neurotic person is a malingerer. To just the extent that he is conscious of this does the neurotic patient deserve to share in the opprobrium that attaches to malingering. Freud discussed this in the account of Dora, his first reported history of a case (Collected Papers,[8] vol. 3, p. 52). Dora made bitter reproaches against her father, charging among other things that he was malingering, in that he used tuberculosis to justify expeditions with a woman who was at the same time his nurse and his mistress. This reproach, as Freud pointed out, while true, actually rose out of her own bad conscience, and was a self-reproach not only for earlier states of ill health—aphonia, coughing, etc.—but also for more recent ones. What she hoped to gain by her immediate illness, Freud pointed out to her, was to detach her father from his mistress, something she had been able to achieve by no other method. Thus she was also malingering. "I felt quite convinced," said Freud, "that she would recover at once if only her father were to tell her that he had sacrificed Frau K for the sake of her (Dora's) health, but I added that I hoped he would not let himself be persuaded to do this, for then she would have learned what a powerful weapon she had in her hand, and she would certainly not fail on every future occasion to make use once more of her liability to ill health." (This, as is known, is precisely what neurotic families encourage certain members of the family to do.) Freud continued that those "crudest and most commonplace views" of hysterical disorders i. e., that they could be cured by some catastrophe, are in a certain sense correct, but that they overlook psychologic distinctions between what is conscious and what is unconscious. One can say that the neurosis always contains a certain amount of malingering, i. e., a certain amount of conscious secondary gain from the elements, although in some instances this amount may be very small.

5. Jones, A. Bassett, and Llewellyn, Llewellyn J.: Malingering, Philadelphia, P. Blakiston's Son & Company, 1917.

malicious and unintentional deception in disease. The authors assume it to be self-evident that the malingerer's behavior, and therefore his intention, is morally reprehensible and that his success in concealing its factitious origin is even more so. The moral attitudes of condemnation follow naturally from the assumption that the immediate and sole purpose of the simulation is material gain.

It would seem evident that, as to the moral reprehensibility of the malingerer, the scientist has no more justification for forming an opinion than in the case of any other clinical phenomena. The medical scientist is fairly entitled to judge as to whether or not a given condition is injurious to society; he is justified, for example, in quarantining a patient with smallpox. But to decide as to the morality of the illness has never been the physician's function. He does not attempt, for example, to pass on the sinfulness of syphilis. The scientist who becomes angry with the subject of his investigations is to that extent no longer scientific.

How then can one interpret the curious attitude which may be detected in those who write on malingering, and in the way in which physicians, lawyers, and employers discuss such cases?

The first explanation lies in the widespread fallacy of assuming that conscious motives can be regarded as explanatory of human behavior. Especially is this lost sight of by medical writers who, accustomed to deal with physiologic functions over which the conscious intention has a minimum of authority, turn on rare occasion to the analysis of behavior. Behavior cannot be understood in terms of conscious intention alone; unless one considers the unconscious motives which determine an act one cannot understand the significance of the act to the actor.

A second reason for the irritation exists, however. Intuitively physicians grasp one of the unconscious motives of malingering without clearly recognizing it intellectually; they react to it emotionally. For a man to injure himself so that he escapes responsibility or obtains money is reprehensible from the standpoint of the employer and of society at large. It is an aggression against society, although done in the form of an aggression against the self. But this is not sufficient reason for the many aroused emotions of the physician; he is only too familar with many examples of aggression against society in the form of sickness. The shoe pinches because malingering is also an aggression against the physician himself. It is an attempt to deceive him, to perplex, perhaps to overtax and ridicule his diagnostic acumen and his therapeutic efforts. If one reads the reports of cases of malingering, one cannot but be struck by the frequency with which the physician describes how a certain wound, for example, is almost healed time after time, only to show exacerbation which puzzled all the consultants.

When at last the factitious nature of the injury is discovered, there is almost a shout of triumph in the clinical reports, and some authors even describe how the patient was reproached, sharply spoken to, summarily dismissed or otherwise punished. It is this which clearly indicates that the physician recognizes intuitively that one of the motives of the patient was not so much the material gain as the unconscious wish to fool the physician and, coincidentally, to make a bid for punishment.[6]

One often sees the same aspect of this phenomenon clearly demonstrated in the course of psychoanalytic treatment. The patient begins to give evidence of regarding the treatment as a competitive struggle with the analyst. This may be subtle, or the patient may frankly announce it. "You have got to yield; I never will," said one of my patients, clearly recognizing, even as he said it, that it was a defensive and, at the same time, aggressive gesture. Such patients are like the skeptic described by Karin Stephen[7] who, when told of the significance of slips of the tongue, declared, "One or two instances like that would never convict (convince) me."

Such a competition with the analyst takes this specific form: "You may be a wise and highly regarded analyst, but now you have met your match. I will show you that you can't cure me." Such dreams as the following are familiar to all analysts: A baseball game is in progress. A man resembling the analyst is the pitcher, and he has achieved a remarkable record. He has struck out nearly every batter that has faced him. The dreamer goes to bat and knocks a home run (he is going to give up the analysis and go home). Or, in another and still more specific dream he steps up to the plate and knocks foul after foul so that the pitcher, in spite of his wonderful record, is unable to fan him out and is, on the other hand, worn out with the contest. In such a dream it is almost self-evident the foul balls are the unscrupulous devices for resistance used by the patient to prolong and stalemate the analysis, exhaust the patience of the analyst and provoke his exasperation.

From this, one can hazard the assumption that the original act of malingering serves chiefly as a provocative aggression, i. e., that it is a minor self-attack designed to excite a major attack from another person. In this it corresponds to the criminality from a sense of guilt described by Freud[8] and elaborated by Alexander.[9]

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6. So dogged is this refusal to confess the deception that patients will go to incredible lengths in their submission to treatment. I know of the case of a man and woman who claimed to have effected a suicide pact and to be dying of self-inflicted poison. They were taken to a hospital and given heroic treatment with a powerful antidote which resulted in their deaths, and it was not until shortly before death occurred that they confessed that they had not taken poison.

7. Stephen, K.: Psychoanalysis and Medicine: The Wish to Fall Ill, New York, The Macmillan Company, 1933.

8. Freud, S.: Collected Papers, London, Hogarth Press, 1925, vol. 4.

9. Alexander: The Criminal, the Judge and the Public, New York, The Macmillan Company, 1930.

CLINICAL EXAMPLES

Since malingering is usually imitative or simulated, many forms of illness or sickness can be represented, but in general there are two forms: those in which incapacity is claimed because of subjective evidence (for example, the patient insists that he feels too sick to work), and those in which the incapacity is ascribed to an evident local injury which has been self-induced. Only the latter can serve as illustrations of focal self-destruction. I shall cite only a few examples.

The first is that of a woman, aged 29, whom I saw briefly, in consultation with a surgeon who was certain that she had a basal skull fracture. Her pillow was drenched with blood, and she was tossing about as if in great pain, responding to questions in a confused semidelirious fashion. She begged constantly for morphine, which was given her. I incurred the surgeon's displeasure by vetoing his intention to perform a craniotomy immediately on the basis that I was not convinced that there was an intracranial lesion.

After a few days' observation the nurses detected her in the act of picking open small vessels inside the external ear, which was presumably the way in which she had brought about the profuse hemorrhages which, by that time, had almost exsanguinated her.

A few days later she disappeared from the hospital. A month later I was urged by a colleague in another city to come at once in consultation on a case, the description of which made it obvious that it was the same patient.

Later, also, I learned from various sources that she had succeeded in persuading a competent surgeon to do a cranial decompression, and that in several cities she had collected money from insurance companies and corporations, to whom she was able to make it appear that they were in some way responsible for her self-induced injuries.

The elements of aggression, exhibitionism and self-punishment are obvious in this case, in spite of the brief opportunity available for studying it. To say that the patient wanted money, morphine or attention, or all three, is, to say the least, to disregard the extraordinary means which she used to obtain them. It would be accepting the face-saving rationalizations of the ego at par value, in the teeth of striking neurotic stigmas.

What was most enlightening about the case was the effect it produced on the professional men who saw her. The first effect was to create in the nurses and surgeons great interest and concern. As her shocking condition became more apparent, the emotions changed into pity and a strong wish to give her relief. When, however, the nature of her illness became known, the strongly positive feelings were exactly reversed. The surgeon was angry at the deception and was considerably put out with himself for having expended so much time and sympathy and for having been so completely taken in. Under such circumstances one may properly apply a technical device which experience has proved useful in clinical psychoanalysis. When, in spite of one's scientific training and an effort to maintain an objective attitude toward the patient's behavior symptoms, one finds oneself strongly moved emotionally in a certain direction, toward pity or anger or exasperation, it is a useful measure to ask oneself if it is not precisely this result which the patient is unconsciously attempting to produce. One of my patients, for example, who had an indescribably irritating method of picking flaws in whatever I did or said, suddenly stopped short one day in the middle of a harangue to confess that in spite of a conviction of earnestness and sincerity which he felt strongly, he could not deny that as he spoke there flashed across his mind the

image of the leering smile which he gave his father on occasions in his youth when, by similar behavior, he would taunt his father into pursuing and punishing him.

Another typical case was one presented by Dr. Edward Delehanty before the Central Neuropsychiatric Association in September 1929. A youth of about 20 years had, in the course of two years, succeeded in deceiving a dozen physicians with regard to an extensive and crippling burn on his hand and arm. Extensive skin grafting was undertaken time after time; in each instance, after an early show of success, sloughing would reappear. The youth's suffering must have been enormous, and his monetary profit was almost certain to be slight. It was discovered that during all those months he had systematically renewed the wound by surreptitiously annointing the edges with phenol which he purchased for the purpose and kept concealed in his bed. I cannot conceive of an explanation outside of that afforded by this theory for such behavior, which the reports of industrial surgeons, dermatologists and others would indicate to be rather frequent.

A most enlightening contribution to the understanding of malingering comes from the descriptive accounts given by dermatologists of this type of illness, which would appear to be a rather common clinical entity: dermatitis factitia or dermatitis artefacta.[10]

This is a condition in which lesions are voluntarily inflicted on the skin of the person himself, with the aid of corrosive chemicals or mechanical agents such as penknives, fire (particularly from matches), cigarets, the finger or some other object, perhaps most commonly with the finger-nails. I exclude from consideration the cases in which there is an acknowledged compulsion to pick at the skin until the lesion has formed. This is not malingering, since it is not in any sense con-

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10. Duprat, P. E.: Factitious Eruptive Disease, Rev. méd. d. Uruguay **23**:123 (March) 1920; abstr., J. A. M. A. **74**:1748 (June 19) 1920. Short, A. R., and Walker, C. H.: Self-Inflicted Injuries in Civilian Practice, Brit. M. J. **1**:298 (Feb. 26) 1921. Bridge, G. A.: Industrial Malingerer, Southwestern Med. **9**:98 (March) 1925. Grindon, J.: Feigned Eruptions, J. Missouri M. A. **26**:451 (Sept.) 1929. Feller, A.: Kerosene Phlegmon of Skin in Malingerer: A Case, Arch. f. Dermat. u. Syph. **159**:580, 1930. Radaeli, F.: Pathomimesis; Detection of Pseudotumor Caused by Injection of Lysoform (Formaldehyde Soap Solution), Gior. ital. di dermat. e sif. **70**:1102 (Oct.) 1929. Speschilow, P. W.: Structure of Artificial Granulomas Noted Among Soldiers During World War, Frankfurt. Ztschr. f. Path. **38**:513, 1929. Fox, H.: Artificial Dermatitis Due to Plants, Irradiations, Medicaments and Malingering, Proc. Internat. Assemb. Inter-State Post-Grad. M. A. North America **5**:136, 1930. Spillman, L., and Watrin, J.: Cutaneous Self-Mutilation; A Case, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Nancy) **38**:350 (March) 1931. Pautrier, L. M., and Silber, J.: Dermatosis Voluntarily Provoked by Cauterization with Potassium Hydroxide and Necessitating Amputation of Fingers; A Case, ibid. **37**:1216 (Dec.) 1930. Gate, J.; Bosonnet, G., and Michel, P.: Factitia, Cutaneous Pathomimesis: Two Cases, J. de méd. de Lyon **10**:351 (May 20) 1929. Casazza, R.: Cutaneous Pathomimesis in Hysteria, Boll. d. Soc. med.-chir., Pavia **4**:547, 1929. Stokes, J. H., and Garner, V. C.: Diagnosis of Self-Inflicted Lesions of Skin; Contribution to Physical Diagnosis in Dermatology, J. A. M. A. **93**:438 (Aug. 10) 1929. Ribeiro, H.: Unusual Case of Simulation of Dermatosis, Brasil-med. **43**:229 (March 2) 1929. Rasch, C.: Cutaneous Pathomimesis, Ugesk. f. læger **91**:789 (Sept. 19) 1929. Mazzant, C.: Cutaneous Self-Mutilation in a Neurotic; A Case, Dermosifilografo **6**:505 (Sept.) 1931.

cealed, but rather the result of unconscious impulses which a patient cannot explain, but does not deny. What characterizes dermatitis artefacta, as all dermatologists point out, is the persistent denial of authorship, even in the face of absolute proof.

"Many of these patients," Netherton[11] stated, "are subjected to repeated and extensive surgical procedures, and may even suffer irreparable damage and mutilation. In fact many cases are on record in which an arm, finger, etc., have been unnecessarily removed with the full consent of the patient.

"In three of my cases the patient submitted to repeated abdominal operations. Beside the economic loss involved in such cases, the inconvenience sustained by innocent members of the patient's family is frequently little short of tragic."

In these few words this intuitive dermatologist strikes at the psychologic factors which I regard as the most important in malingering: the wish to suffer, the wish to conceal, the wish to injure oneself and, to an even greater extent, the wish to cause other people pain, distress and embarrassment. In other words, there are all the factors one finds in suicide: the wish to hurt oneself, the wish to be hurt and the wish to hurt some one else.

In another study[12] I pointed out how surgical operations are apparently sought and demanded as expression of some unconscious need for self-mutilation at the hands of another person, and I was, therefore, particularly impressed by the observations of Netherton and others that this type of malingering was frequently associated with repeated surgical procedures. In four of the cases Netherton cited, the self-mutilation began after an uneventful appendectomy. The first case is particularly striking, since in this instance six or more major operations were performed subsequent to the original appendectomy, which began the self-induced ulcerations. It was as if the patient was compelled to have an operation made on her abdomen. Six surgical incisions did not suffice; she must continue the process by making innumerable attempts to open her own abdomen by a frustrated and incomplete, but undoubtedly painful, method. Netherton's account of the case leaves little doubt as to the burden which her continued sickness caused her parents. The vicious circle established depended on the fact that by her suffering she simultaneously made the desired aggression against them, atoned for it and justified herself in additional aggressions.

Through the courtesy of Dr. Joseph Klauder of Philadelphia, who has made numerous contributions to the literature on the subject,[13] I was able to study briefly several cases in conference with him. The first patient was a feebleminded woman, who presented lesions regarded as dermatitis factitia, that is, self-produced. They were sharply circumscribed areas, as though produced by the application of a caustic. Dr. Klauder had never been able to obtain much cooperation from the family and could not prove that the lesions were self-produced, although he was sure that they were. The only motive he could elicit was that she was very anxious to be admitted to the hospital. Her sister said that the patient was extremely fond of going to hospitals. An interesting feature about the patient was that she had two fingers amputated, apparently for lesions that were self-produced, as far as the evidence showed.

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11. Netherton, E. W.: Dermatitis Artefacta, with a Report of Seven Cases, Ohio State M. J. **23**:215 (March) 1927.

12. Menninger, K. A.: Polysurgery and Polysurgical Addictions, Psychoanalyt. Quart. **3**:173 (April) 1934.

13. Klauder, Joseph: The Cutaneous Neuroses, with Particular Reference to Psychotherapy, J. A. M. A. **85**:1683 (Nov. 28) 1925.

I am indebted to Dr. Klauder for the account of the following case of the same sort. The patient was a woman of 35 years who, for six months, had had recurrent attacks of a dermatitis. Her husband was insistent that something be done for her, and the family physician sought a consultation with a dermatologist. The dermatologist, in turn, asked Dr. Klauder to see the patient. She presented curious bandlike areas of erythema encircling her wrists like a wristwatch and below the knee like a garter. These led to the diagnosis of dermatitis factitia. When the patient was taking a bath, her room in the hospital was searched, and a bottle of compound solution of cresol was found. Dr. Klauder accused her of producing the lesions with it, but she stoutly denied it. Later she admitted using it to wash her hands and to apply to the skin in order to prevent the skin disease, which she had been told was a streptococcic infection. This was a partial confession of the truth. Her emotional tone was normal, and she presented no neurologic abnormalities, except that her conjunctiva and hard palate were anesthetic. This and the dermatitis artefacta justified the diagnosis of hysteria.

Dr. Klauder discovered that her illness had become "town gossip" in the small town in which she lived. Her family physician had been obliged to issue a daily bulletin as to how she was, in answer to the many inquiries he received as to her progress. She was the recipient of many gifts, flowers and cards, both at her home and after she entered the hospital. She arranged the postcards in a kind of picture-gallery exhibit about her sickroom.

In both of the cases cited it will be observed that the patient endeavored to bring about the confusion and embarrassment of the physicians, as well as to carry out the evident purpose of exciting sympathy and attention. It is particularly desirable to emphasize the absence of any monetary gain, which the industrial surgeon is apt to regard as the only motive for malingering.

It is extremely interesting to compare dermatologic malingering, for which the patient nearly always denies any responsibility, with what dermatologists call neurotic excoriations, several instances of which Dr. Klauder showed me, and in all of which it was frankly confessed by the patient that for reasons unknown to her and beyond her control she was compelled to pick, pinch or dig at herself until various ulcerations were formed. I mention these cases, which in a sense are out of place in a paper on malingering, only to indicate the theoretical distinction between them, namely, that in these self-mutilations the aggression is almost entirely self-directed and not at all provocative, whereas in dermatitis factitia (malingering) the aggression is chiefly intended for another person and, as has been seen before, seems to serve a provocative function.

COMMENT

The chief elements in malingering of the self-mutilative type are: the infliction of a wound on the self which results in pain and loss of tissue; exhibition of the wound to persons who react emotionally to it and give sympathy, attention and efforts to cause healing; the deception of the observer as to the origin of the wound and often distinct efforts to defeat therapeutic measures and the obtaining of monetary or other material reward or detection, exposure, with constant humiliation, reproach and sometimes actual punishment. The cases presented show that one cannot subscribe to so naive a view as that consciously advanced by the detected malingerer, that he was willing to gamble with his chances

in the exchange of a self-inflicted wound for gain. With so much gambling instinct in the race, the infrequency of malingering would, in itself, contradict this interpretation. Again, it is well known that the pain endured is frequently out of all proportion to the anticipated monetary gain. Furthermore, such interpretation ignores the unconscious factors which, however unfamiliar to the malingerer and the public, are now well known to medical science.

The well known disparity between the great suffering voluntarily endured and the objective gain is to be explained on two bases: first, that the gain is only partly represented by the monetary reward, but includes also the satisfactions in exciting sympathy, attention, perplexity and dismay, and, second, the pain is not only incident to the device used for obtaining the gains, but is psychologically demanded by the conscience as a price for indulging in them. Actions speak louder than words, and it is clear that however conscienceless the malingerer appears (or claims) to be, he unconsciously feels guilty and inflicts his own punishment. Unfortunately, there are available as yet no precise instruments with which to measure emotions, but probably there is a precise quantitative relationship, so that the externally achieved punishment is reciprocal with the amount of self-inflicted suffering. The less of one, the more there is of the other. A man who enucleates his own eye meets with less reproach and condemnation than one who burns himself with a match, even though each may do so for the same external purpose. This, to be sure, depends to a large extent on the sense of justice implicit in one, but it is precisely this in every one and in himself that the patient takes advantage of to achieve an equilibrium of emotional forces.

CONCLUSIONS

Malingering, therefore, of the self-mutilative type may be described as a form of localized self-destruction which serves simultaneously as an externally directed aggression of deceit, robbery and false appeal. The aggression is of such an inflammatory sort that it, in turn, obtains for the malingerer not only sympathy, attention and monetary gain (at first), but, ultimately, exposure, reproach and "punishment." Both aspects of the induced treatment by the outside world are strongly tinctured with the perverted erotic satisfaction incident to masochism and exhibitionism.

From this, one may conclude that the original act of malingering of this type serves chiefly as a provocative aggression; i. e., it is a minor self-attack designed to excite a major attack (both indulgent and punitive) from other persons, the pain involved being the price demanded by the conscience for the unconscious satisfactions achieved.

CEREBROSPINAL FLUID IN TUBERCULOUS MENINGITIS

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The cerebrospinal fluid in tuberculous meningitis has been studied since Quincke [1] introduced the method of lumbar puncture in 1891. Denigés and Sabrazés,[2] in 1896, compared the results of chemical analysis of the cerebrospinal fluid in 2 cases of tuberculous meningitis with the values in a case of rabies and suggested that further study would reveal a formula of the chemical changes in the cerebrospinal fluid characteristic of each infection of the central nervous system. Mestrezat and Gaujoux,[3] in 1909, reported findings in 2 cases of tuberculous meningitis confirming the formula of Denigés and Sabrazés.[2] Mestrezat,[4] in 1912, reported cerebrospinal fluid syndromes in a large number of diseases. With rare exceptions his observations have been confirmed. Mestrezat [5] further elaborated these cerebrospinal fluid syndromes on the basis of the physical and chemical characteristics of the fluid.

In 1925, Fremont-Smith and Dailey [6] stated: "It should again be emphasized that a combination of pressure and dynamic studies. cell count, color of fluid, presence and character of clot, determinations of the protein, sugar and chloride values, together with a consideration of the stage of the disease, are necessary to obtain the most information from a lumbar puncture." Fremont-Smith and Ayer,[7] in 1927, and Fremont-Smith,[8] in 1932, published tables of observations on the cerebro-

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1. Quincke, H.: Berl. klin. Wchnschr. **28**:929, 1891.
2. Denigés, G., and Sabrazés, J.: Rev. de méd., Paris **16**:833, 1896.
3. Mestrezat, W., and Gaujoux, E.: Rev. neurol. **17**:733, 1909.
4. Mestrezat, W.: Le liquide céphalo-rachidien normal et pathologique, Paris, A. Maloine et fils, 1912.
5. Mestrezat, W.: Ann. Inst. Pasteur **38**:719, 1924.
6. Fremont-Smith, F., and Dailey, M. E.: Cerebrospinal Fluid Chlorides, Arch. Neurol. & Psychiat. **14**:509 (Oct.) 1925.
7. Fremont-Smith, F., and Ayer, J. B.: Cerebrospinal Fluid in Differential Diagnosis, J. A. M. A. **88**:1078 (April 2) 1927.
8. Fremont-Smith, F.: Cerebrospinal Fluid in Differential Diagnosis of Brain Tumor, Arch. Neurol. & Psychiat. **27**:691 (March) 1932.

spinal fluid in various diseases and once more stressed the diagnostic importance of a quantitative chemical survey of the fluid. The majority of physicians, however, still content themselves with determination of the cell count, a qualitative protein test and the Wassermann test.

During the past ten years we have examined over 15,000 specimens of cerebrospinal fluid at the Massachusetts General Hospital and at the Boston City Hospital. With this background it is our purpose to present the observations on the cerebrospinal fluid in 84 verified cases of tuberculous meningitis (297 fluids). We wish particularly to reemphasize the specificity of the cerebrospinal fluid syndrome in this disease and to demonstrate the value of such syndromes in differential diagnosis.

The series presented is large enough to include important exceptions to the usual picture, and our experience has been sufficiently wide to give us data on conditions which may simulate tuberculous meningitis from either the clinical or the laboratory point of view.

LITERATURE

The literature on tuberculous meningitis is voluminous, but largely limited to the report of a few cases or to the study of one or two constituents of the cerebrospinal fluid. No comprehensive review will be attempted. We shall limit ourselves to a discussion of a few of the more important contributions to the subject.

Mestrezat's studies [9] have already been referred to. His later article [5] is based on observations on 132 fluids from 68 cases of tuberculous meningitis, as well as a review of the observations on more than 200 fluids reported in the literature. His conclusions will be discussed later.

Bickel [10] (1923), in a series of 189 fluids from 80 cases, reported chloride values in 35 fluids and sugar values in 10. Fontecilla and Sepulveda [11] summarized the chloride values in 200 cases (70 verified at autopsy). Nowicka [12] gave chloride values in 60 cases (children). Riser [13] summarized the chloride determinations in 180 cases. Stewart [14] reported quantitative estimations of protein, sugar and chlorides, as well as the cytology and bacteriology in 30 cases (children). Regan [15]

9. Mestrezat (footnotes 4 and 5).
10. Bickel, G.: Schweiz. Arch. f. Neurol. u. Psychiat. **12**:269, 1923.
11. Fontecilla, O., and Sepulveda, M. A.: Le liquide céphalo-rachidien, Paris, A. Maloine et fils, 1921.
12. Nowicka, H.: Arch. de méd. d. enf. **27**:726, 1924.
13. Riser: Le liquide céphalo-rachidien, Paris, Masson & Cie, 1929.
14. Stewart, D.: Edinburgh M. J. **35**:141, 1928.
15. Regan, J. C.: The Human Cerebrospinal Fluid, New York, Paul B. Hoeber, Inc., 1926, p. 314.

reported chloride values in 31 fluids, sugar values in 33 and protein values in 34. Foord and Forsyth,[16] in one of the most important recent communications, reported observations on 147 fluids from 87 proved cases of tuberculous meningitis. The quantity of sugar was determined in 84 fluids and that of chlorides in 65. In addition, cell counts, globulin values and the colloidal gold reaction were studied.

Small series of cases and the lack of wide experience with other conditions have led to dogmatic statements, particularly with regard to chloride values. This will be discussed in detail in the body of the paper.

MATERIAL

The material consisted of 297 fluids from 84 cases of tuberculous meningitis verified by autopsy, inoculation of guinea-pigs or the finding of tubercle bacilli in the clot or centrifugated sediment of the cerebrospinal fluid. We have already reported the observations on the cerebrospinal fluid in 16 of these cases.[17] There were 54 male and 30 female patients, ranging in age from 6 months to 59 years. In many cases lumbar puncture was performed on several occasions. The complete data on the first and the last fluid obtained (145 fluids) are presented in table 1. The data on the 152 additional fluids are included in the other tables.

METHODS

The cerebrospinal fluid pressure was measured with the patient in the recumbent position by the Fremont-Smith modification of the Ayer "water" manometer. The cell count was made in a blood counting chamber after being stained faintly with Unna's polychrome methylene blue (methylthionine chloride, U. S. P.). The protein was determined by the Ayer, Dailey and Fremont-Smith[18] modification of the Denis-Ayer[19] method. The sugar content in the cerebrospinal fluid and in the blood was determined by the method of Folin and Wu,[20] using the modified tubes recommended by Rothberg and Evans.[21] The chloride value in the cerebrospinal fluid and in the serum was determined by the Wilson and Ball[22] modification of the Van Slyke[23] method. The colloidal gold reaction was carried out as described by Cockrill,[24] except that the distilled water was redistilled after adding potassium permanganate, instead of being triply distilled.

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16. Foord, A. G., and Forsyth, A.: Am. J. Clin. Path. **3**:45, 1933.

17. Fremont-Smith, F.; Dailey, M. E.; Merritt, H. H., and Carroll, M. P.: The Equilibrium Between Cerebrospinal Fluid and Blood Plasma: II. Composition of Human Cerebrospinal Fluid and Blood Plasma in Meningitis, Arch. Neurol. & Psychiat. **25**:1290 (June) 1931.

18. Ayer, J. B.; Dailey, M. E., and Fremont-Smith, F.: Denis-Ayer Method for the Quantitative Estimation of Protein in the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **26**:1038 (Nov.) 1931.

19. Denis, W., and Ayer, J. B.: A Method for the Quantitative Determination of Protein in the Cerebrospinal Fluid, Arch. Int. Med. **26**:436 (Oct.) 1920.

20. Folin, O., and Wu, H.: J. Biol. Chem. **38**:81, 1919.

21. Rothberg, V. E., and Evans, F. A.: J. Biol. Chem. **58**:443, 1923.

22. Wilson, D. W., and Ball, E. G.: J. Biol. Chem. **79**:221, 1928.

23. Van Slyke, D. D.: J. Biol. Chem. **58**:523, 1923.

24. Cockrill, J. R.: Comparison of Gold Chloride, Benzoin and Mastic Tests on Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **14**:455 (Oct.) 1925.

Pressure.—The cerebrospinal fluid pressure was measured in 218 instances. The pressure varied between 35 and 800 mm. of cerebrospinal fluid, with an average of 375 mm. The cerebrospinal fluid pressure at the first puncture was recorded in 61 cases; in 81 per cent the pressure was greater than 200 mm., in 63 per cent greater than 300 mm., in 31 per cent greater than 400 mm. and in 5 per cent greater than 600 mm. There were only 11 patients (19 per cent) with a pressure less than 200 mm. In 8 of these subsequent punctures were made, and in all but 1 the pressure had risen to over 200 mm. With progress of the disease there was usually an increase in the pressure. A few patients showed lower pressure on subsequent punctures. This was usually due to the short interval between punctures. Occasionally the low pressure resulted from the development of spinal subarachnoid block.

Appearance.—The fluid in most instances was clear. It was nearly always a faint yellow. This is often overlooked unless the fluid is compared with tap water. The fluids which contained a large number of cells usually had a "ground glass" appearance. No frankly purulent fluids were encountered. A fine fibrin clot was noted in 124 fluids (43 per cent). A greater percentage would probably have shown a clot if a sample of fluid had been set aside regularly for this purpose. The literature is consistent in stating that a fine clot nearly always forms if the fluid is allowed to stand. In several fluids the syndrome of Froin was present.

Cells.—The white cell count in 253 fluids (83 cases) varied between 5 and 2,021 cells per cubic millimeter, with an average of 265. In the majority of cases a few red blood cells were also seen. The fluid usually showed moderate pleocytosis. In 85 per cent the cell count was between 50 and 500. In only 9 per cent was the cell count over 500, and in 6 per cent it was less than 50. In 2 cases the cells numbered less than 25 (cases 39 and 67, with counts of 10 and 5, respectively). In both cases the number of cells increased to over 25 in subsequent punctures. Adults tended to show a higher cell count than children. In the 141 fluids in which a differential count was recorded there was a preponderance of polymorphonuclear leukocytes in only 16 instances. In the remainder lymphocytes predominated. Polymorphonuclear cells were present in most fluids, averaging 20 per cent.

Protein.—The protein content in 253 fluids from 78 cases varied between 25 and 1,142 mg., with an average of 200 mg., per hundred cubic centimeters. The ranges of protein values were: less than 45 mg., 1 per cent; 45 to 100 mg., 27 per cent; 100 to 200 mg., 38 per cent; 200 to 500 mg., 29 per cent, and more than 500 mg., 5 per cent. In only 2 instances was a normal value (45 mg. or less) obtained. In 1 of these (value 43 mg.) only one puncture was made; in the other (case 82) an original protein value of 25 mg. rose to 90 mg. on a subsequent puncture. Ninety-four per cent of the fluids showed a protein content between 45 and 500 mg. Values over 500 mg. (in 12 fluids) were usually due to the development of subarachnoid block.

Sugar.—The sugar content of the 222 specimens of spinal fluid drawn off by lumbar puncture from 73 patients varied between 5, or less, and 59 mg., with an average of 28 mg., per hundred cubic centimeters. Only 17 fluids of the total 222 had values of 50 mg. or higher, and only 35 fluids had values of 45 mg. or higher. Ninety-three per cent of the values were below 50 mg., 84 per cent below 45 mg., 77 per cent below 40 mg., 57 per cent below 30 mg., 28 per cent below 20 mg. and 5 per cent below 10 mg.

TABLE 1.—*The Cerebrospinal Fluid in Eighty-Four Cases of Tuberculous Meningitis*

Case	Sex, Age	Date	Pressure, Mm. of Cerebrospinal Fluid	Clot	White Cells, per Cu.Mm.		Protein, Mg. 100 Cc.	Sugar, Mg. 100 Cc.	Chloride,* Mg. 100 Cc.	Colloidal Gold Curve	Confirmation of Diagnosis
					Number	Per Cent Polymorphonuclears					
1. G. A.	M 55	11/ 9/25	170	0	...	..	100	47	...	0000000000	Autopsy
		11/18/25	230	0	250	1	211	30	...	0000000000	
2. H. A.	M 24	1/30/25	340	+	290	..	364	..	...	0000000000	Smear † and autopsy
3. I. A.	M 27	8/ 6/31	160	+	62	12	294	20	660	0001111000	Smear
		8/14/31	300	+	85	15	210	30	623	.....	
4. S. A.	M 21	11/23/31	490	+	190	10	59	17	601	0000000000	Smear and autopsy
		12/ 6/31	500	0	270	..	193	28	493	.....	
5. E. B.	F 2	5/ 1/25	300	0	150	25	160	41	...	0002222200	Autopsy
		5/ 6/25	400	+	62	..	...	..	...	.....	
6. L. B.	F 49	9/20/27	...	+	247	14	103	28	635	1124554100	Guinea-pig
		9/23/27	...	+	...	..	84	25	732	.....	
7. X. B.	M 19	12/ 2/23	280	0	165	40	333	20	...	0000000000	Smear
8. B. B.	F 6½	3/16/31	...	+	252	0	228	35	610	0001122211	Autopsy
9. R. B.	M 2	2/22/32	180	0	33	0	69	43	619	0112333210	Autopsy
10. M. B.	F 24	4/ 2/25	300	+	600	30	279	27	507	0111233310	Smear and guinea-pigs
11. M. B.	F 18	8/ 6/29	400	0	300	15	...	29	509	5554333332	Smear and autopsy
		8/ 6/29	650	0	440	20	269	24	511	0001123321	
12. E. B.	M 25	1/28/31	520	0	96	..	154	21	570	0001233210	Autopsy
		2/ 9/31	...	0	...	..	354	16	535	0000123221	
13. J. C.	M 2	9/29/27	...	+	189	0	288	26	623	.....	Autopsy
		10/ 3/27	...	0	204	0	211	11	536	.....	
14. E. C.	M 26	7/12/25	175	0	190	..	138	54	668	0000111000	Guinea-pigs
		7/21/25	390	0	376	..	156	22	586	0011222110	
15. P. C.	M 59	3/23/30	90	+	80	..	43	53	...	.....	Autopsy
16. G. C.	F 1½	4/ 5/30	670	0	160	15	147	..	518	0111000000	Guinea-pigs
		4/ 7/30	...	0	...	..	273	14	527	.....	
17. J. D.	F 47	7/21/31	370	+	144	25	142	26	553	0000221000	Autopsy
18. D. D.	M 35	6/30/29	380	0	...	..	200	48	682	1123333344	Autopsy
		7/12/29	450	0	83	..	62	..	623	0112332210	
19. F. D.‡	M 47	11/ 6/27	500	+	270	25	498	20	559	5555544210	Autopsy and guinea-pigs
		11/ 8/27	...	+	...	..	510	9	574	.....	
20. E. D.	F 32	3/ 7/22	...	0	450	64	250	..	...	.....	Guinea-pigs
		3/ 9/22	...	+	300	..	...	..	...	.....	
21. I. F.	F 5	3/18/31	...	0	107	..	129	..	...	0012443332	Autopsy
22. M. G.	M 33	6/11/30	...	+	31	9	166	10	...	1111233332	Guinea-pigs
		6/14/30	...	0	612	..	414	5	570	.....	
23. J. G.	M 26	2/15/26	220	+	210	..	228	35	...	0000111000	Smear and guinea-pigs
		2/16/26	...	+	...	..	206	46	...	0000112211	
24. R. G.	M 48	3/25/30	150	0	460	0	133	40	720	1112222222	Smear
		3/31/30	550	+	578	..	282	16	680	0001222221	
25. F. G.	F 37	9/18/21	...	0	84	..	...	..	...	.....	Smear and guinea-pigs
26. M. G.	F 16	8/12/30	350	0	162	..	88	22	622	1112321100	Smear
		8/15/30	650	+	...	..	114	..	579	0001221000	
27. J. G.	F 22	12/ 9/24	440	+	86	25	63	35	661	1223221000	Smear
		12/18/24	...	0	...	..	250	17	603	0000112333	
28. R. G.	M 14	7/28/29	370	0	320	0	120	..	...	0112333210	Guinea-pigs
		8/ 1/29	750	0	...	..	156	19	...	1122322210	
29. A. H.	M 8	3/31/23	...	0	320	..	...	..	...	.....	Smear
30. M. H.	F 21	10/25/31	350	+	100	14	...	59	706	.....	Smear
		11/ 4/31	650	+	480	..	138	45	553	.....	
31. B. H.	M 1	8/ 4/24	...	+	150	30	143	19	...	0124321000	Autopsy
32. L. H.§	M 24	2/29/24	210	0	350	..	80	60	...	1133311100	Smear
		3/ 7/24	380	0	306	4	95	45	...	1133320000	
33. X. H.	M 1	9/28/23	...	0	75	..	91	54	...	0000000000	Autopsy
		10/ 4/23	...	0	...	..	308	26	...	.....	
34. C. H.	M 31	5/29/25	160	0	108	30	93	41	679	0001222000	Smear
		6/15/25	350	0	160	7	296	27	515	0000012110	
35. A. K.	M 55	8/ 2/29	290	0	600	44	296	35	597	1112233321	Autopsy
		8/ 4/29	100	+	...	..	364	26	592	0122233210	
36. W. K.	M 24	10/26/25	...	+	...	..	206	22	589	0001113221	Autopsy
		10/28/25	430	0	54	..	279	21	564	0000112311	
37. X. K.	M 4	4/ 8/26	280	0	1,100	0	192	10	597	0000112221	Autopsy
38. M. K.‖	M 46	7/26/32	...	0	160	..	89	56	653	.....	Autopsy
		8/ 4/32	70	0	...	..	53	39	640	.....	
39. M. L.	F 43	3/14/30	250	+	10	..	56	33	627	0122100000	Autopsy
		3/19/30	50	+	32	..	100	5	560	1112333321	
40. E. L.	F 22	7/13/29	380	0	70	0	57	..	676	0123333210	Autopsy
		7/17/29	250	+	190	70	98	50	579	1112333221	
41. B. L.	M 1	4/10/24	...	0	90	0	286	33	...	.....	Smear
		4/11/24	...	+	100	0	308	..	...	.....	
42. A. M.	M 24	5/15/30	420	+	402	0	138	27	609	.....	Autopsy
		5/18/30	370	0	373	0	150	13	552	.....	
43. X. M.	M 18	4/12/23	180	+	106	53	500	9	...	0001122222	Smear
44. C. M.	M 6	7/18/26	...	0	27	20	77	24	471	5224322110	Guinea-pigs
45. F. M.	F 17	8/21/32	300	+	833	76	75	40	502	0000111000	Autopsy
		8/29/32	500	+	1,740	80	228	27	522	.....	
46. D. M.	F 7	5/30/31	550	0	212	58	167	37	537	0011222211	Smear
		6/ 2/31	550	+	278	..	342	24	542	0012332110	
47. X. M.	M 3	3/28/22	300	0	119	50	...	..	...	.....	Smear
		3/30/23	...	0	55	..	...	..	...	.....	

TABLE 1.—*The Cerebrospinal Fluid in Eighty-Four Cases of Tuberculous Meningitis—Continued*

Case	Sex, Age	Date	Pressure, Mm. of Cerebrospinal Fluid	Clot	White Cells, per Cu. Mm.		Protein, Mg. 100 Cc.	Sugar, Mg. 100 Cc.	Chloride,* Mg. 100 Cc.	Colloidal Gold Curve	Confirmation of Diagnosis
					Number	Per Cent Polymorphonuclears					
48. C. M.	M 18	8/26/26	...	0	98	10	122	49	722	0223430000	Smear
		9/ 2/26	700	0	453	..	138	37	576	0012332000	
49. R. M.	M 22	1/18/27	500	+	408	40	234	29	565	0011221000	Autopsy
50. J. M.	M 35	11/ 2/30	600	0	265	2	...	..	604	.....	Autopsy
51. E. N.	M 20	2/ 8/24	200	+	180	..	250	51	...	1123211000	Smear
		2/15/24	360	+	61	..	362	22	...	1113322000	
52. J. N.	M 24	1/15/24	520	+	700	0	800	21	...	0001110000	Guinea-pigs
		1/21/24	240	0	500	..	1,142	23	...	.....	
53. D. O.	M 1	5/15/23	...	0	62	50	...	..	...	.....	Smear and autopsy
		5/16/23	...	0	68	..	...	..	...	.....	
54. D. O.	F 5	6/14/31	...	0	54	..	62	15	570	.....	Autopsy
		6/18/31	...	0	72	..	143	9	579	.....	
55. L. P.	M ½	6/22/24	280	+	72	58	303	12	...	1222331100	Autopsy
		6/23/24	...	+	70	..	438	15	...	1222233333	
56. C. P.	M 33	8/ 1/23	370	+	259	7	800	20	...	0000000000	Smear
57. L. P.	M 1	6/ 9/30	...	0	190	..	133	20	622	0011210000	Autopsy
		6/12/30	...	+	34	..	252	19	697	.....	
58. E. P.	M 22	10/ 5/27	370	0	390	23	470	14	603	.....	Smear
		10/ 7/27	370	+	410	15	330	11	587	.....	
59. H. P.	F 13	3/14/23	...	0	130	0	...	..	...	.....	Guinea-pigs
		3/20/23	...	0	130	..	...	..	...	.....	
60. J. P.	M 2½	7/22/29	550	0	200	0	103	34	...	1123333221	Autopsy
		7/23/29	...	0	140	..	146	15	602	1222333321	
61. A. P.	F 15	6/10/23	230	0	227	20	174	15	...	1123330000	Autopsy
		6/14/23	290	0	210	1	190	21	...	0001231100	
62. X. R.	M 37	12/ 9/23	300	0	280	3	200	31	...	0000000000	Autopsy
		12/14/23	240	0	255	9	364	30	...	0000000000	
63. F. R.	F 1½	3/ 8/29	550	0	250	80	66	29	603	1122331100	Autopsy
		3/12/29	...	0	75	0	148	17	627	0122444333	
64. F. R.	M 30	8/21/23	330	0	198	66	...	..	...	.....	Smear and autopsy
		8/31/23	260	+	329	44	500	10	...	0000455442	
65. B. R.	F 3	3/11/30	420	+	300	0	153	18	622	2223322221	Guinea-pigs
		3/17/30	...	0	340	..	65	18	648	0123332100	
66. W. R.	F 4	3/26/30	...	+	150	0	133	10	692	0122333332	Guinea-pigs
		4/ 1/30	250	+	150	..	125	14	671	.....	
67. F. S.	M 45	8/23/29	350	0	5	..	204	45	580	1122221000	Guinea-pigs
		8/26/29	350	+	216	..	...	..	...	.....	
68. H. S.	M 53	10/ 7/27	175	0	157	13	216	30	533	.....	Autopsy
		10/10/27	300	0	95	0	143	39	575	.....	
69. S. S.	M 14		390	0	210	5	400	35	...	0012333210	Guinea-pigs
70. E. S.	M 23	8/ 1/24	400	0	84	12	125	32	...	1112444210	Autopsy
71. C. S.	F 29	4/13/25	425	+	64	0	182	20	624	0001111000	Smear
		4/15/25	360	0	35	..	190	20	565	0012231110	
72. B. S.	F 31	11/ 8/27	740	+	59	6	186	21	618	.....	Guinea-pigs
		11/10/27	...	+	186	22	168	11	621	.....	
73. N. T.	F 2½	4/ 9/22	300	0	228	..	...	..	...	.....	Autopsy and guinea-pigs
74. L. T.	M 1	2/15/31	300	+	190	0	148	19	...	0012232100	Guinea-pigs
		2/18/31	...	0	456	0	207	18	697	0001122211	
75. O. T.	F 4	11/ 5/28	...	+	220	..	150	47	642	0012333211	
76. X. T.	M 22	12/ 5/24	210	0	475	..	90	34	649	1122331000	Guinea-pigs
		12/ 9/24 (Lumbar)¶	35	0	90	..	572	56	...	5555553333	Guinea-pigs
		12/ 9/24 (Cisternal)§	390	0	41	..	19	71	696	0111111000	
77. S. T.	F 38	10/14/24	470	0	120	55	600	13	623	0000112332	Smear
78. L. V.	M 10	7/15/29	...	0	250	0	104	52	632	0123333222	Autopsy
		7/23/29	...	+	360	0	116	36	526	0122333221	
79. B. V.	F 22	4/28/25	260	0	189	20	138	29	668	0012322111	Autopsy
		5/ 7/25	530	0	1,017	40	286	15	659	1222343321	
80. G. V.	M 2½	2/ 5/25	...	0	240	..	286	..	...	0011222321	Smear
		2/ 6/25	...	0	251	10	206	18	591	.....	
81. J. W.	M 26	10/ 2/28	350	0	248	0	572	..	577	0001222211	Smear
82. G. W.	M 24	7/22/31	220	0	68	14	25	50	667	0112221000	Autopsy
		8/ 3/31	450	+	144	..	90	39	604	.....	
83. J. W.	M 29	4/ 2/30	170	+	480	..	132	23	604	.....	Autopsy
		4/ 9/30	490	+	339	25	108	29	636	.....	
84. T. Y.	M 34	9/23/30	160	+	...	..	133	42	..	.....	Autopsy
High.....	59		750		1,740	80	1,142	59	732		
Low.....	0.5		35		5	0	25	5#	471		
Average...	21		350		243	19	220	28	604		

* As sodium chloride.

† Tubercle bacilli seen on a stained smear.

‡ The Wassermann reactions of the blood and cerebrospinal fluid were positive.

§ Cisternal fluid was not used in the averages.

‖ A tuberculoma was removed from the left frontoparietal region on March 31, 1932. Numerous lumbar punctures had been done since. The fluid on July 24 showed a sugar content of 28 mg. per hundred cubic centimeters.

¶ Lumbar and cisternal fluids showed complete subarachnoid block.

#Sugar values of 5 mg. per hundred cubic centimeters or less cannot be determined accurately.

There is usually a progressive decrease in the sugar content as the disease advances. This is shown in figure 1, in which the sugar contents at the first and last punctures in 45 cases are compared. Thus, at the first puncture 53 per cent showed a sugar content below 30 mg. as against 75 per cent at the last puncture. Similarly, only 2 per cent (1 case) showed a sugar content of 50 mg. or more at the last puncture as compared with 16 per cent (7 cases) at the first puncture. The average value at the first puncture was 31 mg., while at the last puncture it was 23 mg. per hundred cubic centimeters. In case 32, not included in table 6, cisternal fluid sugar was 60 mg. at the first puncture and 45 mg. at the last puncture (table 1). However, a progressive decrease in the sugar content is not invariable, as is shown in cases 4 and 23. Cases 30 and 82 (table 5) also showed a sharp rise in the sugar level late in the disease. This is probably due to hyperglycemia.

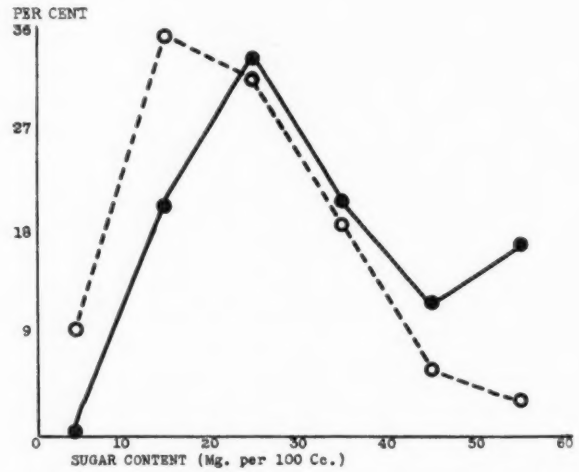

Fig. 1.—A comparison of the sugar contents at the first and last puncture in 45 cases of tuberculous meningitis. The solid line represents the content at the first puncture; the broken line, that obtained at the last.

TABLE 2.—*The Influence of the Serum Sugar Level on the Cerebrospinal Fluid Sugar (Case 12, After Fasting)*

Date	Serum Sugar, Mg. 100 Cc.	Cerebrospinal Fluid Sugar, Mg. 100 Cc.	Date	Serum Sugar, Mg. 100 Cc.	Cerebrospinal Fluid Sugar, Mg. 100 Cc.
1/29/31	148	26	2/3/31	211	32
1/30/31	138	12	2/5/31	134	15
1/31/31	178	24	2/6/31	132	21

In 18 cases the serum or plasma sugar content was determined thirty-four times and the sugar content of the whole blood five times, to compare with the spinal fluid sugar values. The serum or plasma values ranged from 96 to 240 mg. per hundred cubic centimeters, with an average of 135. In 9 instances the values were above 150 mg. per hundred cubic centimeters. The whole blood sugar

values ranged from 84 to 155 mg. per hundred cubic centimeters, with an average value of 128 mg. These figures demonstrate that the low spinal fluid sugar values are not a reflection of a low blood sugar level but occur in spite of a normal or even elevated blood sugar level. In 2 patients with serum sugar levels of 240 and 211 mg., respectively, the corresponding spinal fluid sugar values were 25 and 32 mg. On the other hand, an elevated blood sugar level may be reflected in the cerebrospinal fluid sugar level in spite of the local glycolysis. This is illustrated in case 12, table 2. A rise in the serum sugar value from 138 to 211 mg. was accompanied by a rise in the spinal fluid sugar value from 12 to 32 mg. When the serum sugar value again fell to 134 mg., the spinal fluid sugar value fell to 15 mg. When the blood sugar level is distinctly elevated, the fall in the spinal fluid sugar level may be delayed. In case 76, with a serum sugar level of 178 mg., there was a sugar value of 56 mg. in the lumbar spinal fluid and a value of 71 mg. in the cisternal fluid. On the following day the sugar value in the cisternal fluid fell to 35 mg. per hundred cubic centimeters.

Chlorides.—The chloride content was determined in 91 of the fluids referred to in table 1 and also in 111 fluids obtained at other punctures in the same cases, making a total of 202 chloride determinations in 54 cases. The results varied between 471 and 732 mg., with an average of 605 mg. per hundred cubic centimeters. Values of 700 mg. or higher occurred in 7 instances, only 3 being above 708 mg. per hundred cubic centimeters. The chloride content was below 700 mg. per hundred cubic centimeters in 97 per cent of the fluids, below 650 mg. in 78 per cent, below 600 mg. in 43 per cent, below 550 mg. in 15 per cent and below 500 mg. in 1 per cent. In 63 per cent of the fluids the chloride value lay between 550 and 650 mg. per hundred cubic centimeters.

There is usually a progressive decrease in the chloride level as the disease advances. Only 2 patients (cases 74 and 79) failed to show a chloride value below 650 mg. at some time. In case 74 only 1 chloride determination was made, with a value of 697 mg. In case 79 four punctures were made, with values ranging from 659 to 673 mg. per hundred cubic centimeters. Figure 2 shows a comparison of the chloride levels at the first and last punctures in 37 cases. The average value at the first puncture was 623 mg. and at the last puncture 590 mg. per hundred cubic centimeters. At the first puncture 65 per cent had a chloride content below 650 mg. and 27 per cent below 600 mg., as compared with 86 per cent below 650 and 62 per cent below 600 mg. at the last puncture. In only 1 case did fluid obtained at the last puncture have a chloride content of over 700 mg. (case 6, table 3). Similarly, in 35 per cent of the cases the chloride value was 650 mg. or more at the first puncture, while in only 14 per cent was such a value obtained at the last puncture. A progressive fall in the chloride level, however, is not invariable (cases 6 and 57).

Serum Chlorides.—The accepted normal range for serum chlorides [25] is from 570 to 620 mg. per hundred cubic centimeters. In a series of 80 fasting patients with serum chloride levels varying between 569 and 623 mg. (average 594 mg.), with essentially normal cerebrospinal fluid, we found [26] that the chloride values

25. Myers, V. C.: J. Lab. & Clin. Med. **5**:343, 418 and 590, 1920.

26. Fremont-Smith, F.; Dailey, M. E.; Merritt, H. H.; Carroll, M. P., and Thomas, G. W.: Equilibrium Between Cerebrospinal Fluid and Blood Plasma: I. Composition of Human Cerebrospinal Fluid and Blood Plasma, Arch. Neurol. & Psychiat. **25**:1271 (June) 1931.

in the cerebrospinal fluid varied between 697 and 748 mg. per hundred cubic centimeters, with an average of 726 mg. This may be taken as the normal range of cerebrospinal fluid chloride values in fasting patients with normal serum chloride levels.

We have determined the serum chloride level at the time of lumbar puncture thirty-nine times in 16 patients with tuberculous meningitis. The values varied between 391 and 611 mg., while the cerebrospinal fluid chloride levels in this group varied between 515 and 732 mg. per hundred cubic centimeters. The relation of the cerebrospinal fluid chloride level to the serum chloride level is illustrated in figure 3. The serum chloride level is nearly always decreased in tuberculous meningitis, being below 550 mg. in 85 per cent (all but 6) and below

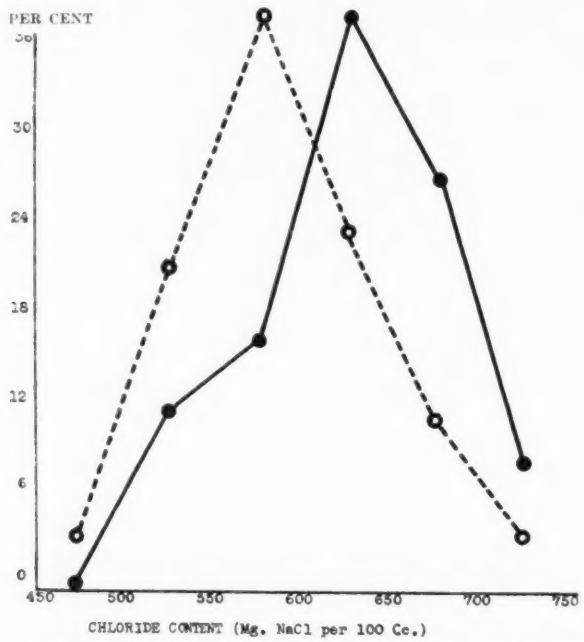

Fig. 2.—A comparison of the chloride contents at the first and last puncture in thirty-seven cases of tuberculous meningitis. The solid line represents the chloride content at the first puncture, and the broken line, that obtained at the last puncture. The black circles indicate serum; the white circles, cerebrospinal fluid.

500 mg. in 46 per cent of the determinations. As we have pointed out previously,[27] this decrease in the serum chloride content, which occurs in all forms of acute meningitis, is the chief reason for the lowering of the cerebrospinal fluid chloride level. Other factors, usually playing only a minor rôle in this decrease in cerebrospinal

27. (*a*) Fremont-Smith, F.; Thomas, G. W.; Dailey, M. E., and Carroll, M. P.: Brain **54**:303, 1931. (*b*) Fremont-Smith, F.: Pathogenesis of the Changes in Cerebrospinal Fluid in Meningitis, Arch. Neurol. & Psychiat. **28**:778 (Oct.) 1932. (*c*) Fremont-Smith and Dailey.[6] (*d*) Fremont-Smith, Dailey, Merritt and Carroll.[17]

fluid chloride level, are the increase in cerebrospinal fluid protein and the increase in cerebrospinal fluid acidity occurring in meningitis.[28]

Four cases in which the serum and cerebrospinal fluid chloride levels were determined repeatedly are presented in table 3. These illustrate the influence of the serum chlorides on the cerebrospinal fluid chlorides. With rare exceptions the direction of change of cerebrospinal fluid chlorides can be accounted for by the change in the serum chlorides. Case 6 in this table shows a rise in serum chlorides which explains the progressive rise in cerebrospinal fluid chlorides. This is the only case in which the cerebrospinal fluid chloride value at the last puncture was above 700 mg. per hundred cubic centimeters, as well as the only case in which the serum chloride level was at any time higher than 573 mg.

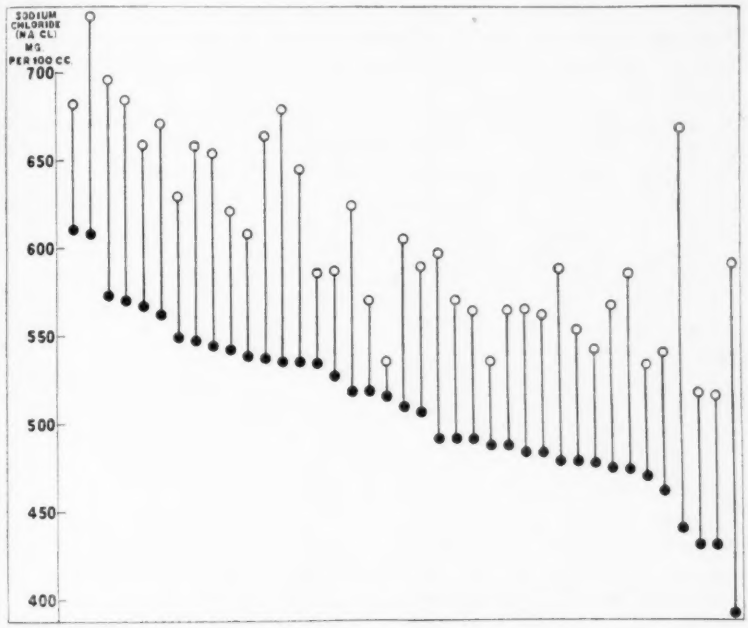

Fig. 3.—The relation of the cerebrospinal fluid chloride level to the serum chloride level in tuberculous meningitis.

Colloidal Gold Curve.—The colloidal gold curve was determined in 116 fluids (68 cases). In 1 case (case 44) the curve was bizarre. Seventeen per cent showed no change in the colloidal gold curve; 2 per cent showed a first zone curve (dementia paralytica); 71 per cent showed a midzone curve (syphilitic), and 10 per cent showed an end 1-zone curve (meningitic). Of the 4 patients showing a first zone gold curve, 3 gave negative reactions to Wassermann tests of the cerebrospinal fluid. The fourth (case 19) gave a positive Wassermann reaction in both the blood and the cerebrospinal fluid.

Wassermann Reaction.—The Wassermann reaction of the cerebrospinal fluid was tested in 60 of the 84 cases. The reaction was positive in 2 cases (19 and 68) and doubtful in 1 (case 58). The Wassermann reaction of the blood was positive

28. Fremont-Smith and Dailey.[6] Fremont-Smith.[27b]

in case 19 and negative in cases 58 and 68. For 24 patients the Wassermann test was not done. Eighteen of these 24 were children.

Bacteriology.—In the majority of cases the fluids were cultured on routine mediums, but no growth was noted. The inoculation of guinea-pigs with fluid from 24 patients yielded positive results in 22 instances. In 2 cases the results of the inoculation were negative, although the diagnosis was confirmed at autopsy. Tubercle bacilli were demonstrated in stained smears of the clot or of the centrifugated sediment in 30 (36 per cent) of the 84 cases.

The demonstration of the tubercle bacillus in the cerebrospinal fluid establishes the diagnosis. The organism can be found in nearly every case if the search is sufficiently diligent. It is best to use the last fluid removed or fluid obtained at cisternal puncture, and to search for the organism in the clot, if one forms. If no clot forms, the overlaying of 5 or 10 cc. of the cerebrospinal fluid with 1 or 2 cc. of 95 per cent alcohol, so that the alcohol mixes with only the upper portion of the cerebrospinal fluid, gives a heavy protein precipitate, which on centrifugation

TABLE 3.—*The Influence of the Serum Chlorides on the Cerebrospinal Fluid Chlorides*

	Date	Serum Chloride,* Mg. 100 Cc.	Cerebrospinal Fluid Chloride,* Mg. 100 Cc.		Date	Serum Chloride,* Mg. 100 Cc.	Cerebrospinal Fluid Chloride,* Mg. 100 Cc.
Case 6	9/20	...	635	Case 30	10/26	570	684
	9/21	547	658		10/27	544	654
	9/22	611	682		10/28	535	645
	9/23	608	732		10/31	461	540
					11/ 4	478	553
Case 12	1/28	491	570				
	1/29	491	597	Case 34	5/29	535	679
	1/30	509	605		6/ 2	537	664
	1/31	478	588		6/13	430	517
	2/ 3	483	562		6/15	430	515
	2/ 5	474	567				
	2/ 6	487	535				

* As sodium chloride.

carries the bacilli to the bottom of the test tube.[29] (The protein precipitate can be thickened if necessary by the addition of a drop of egg albumin.) After staining, the smear should be thoroughly decolorized with acid alcohol (5 per cent hydrochloric acid in 95 per cent alcohol), followed by decolorization with 30 per cent nitric acid for from fifteen to thirty seconds.

Prolonged and repeated search is often necessary before the organism is found. This and the fact that tuberculous meningitis cannot be excluded by the failure to find the organism make the search for the organisms in smear often of little practical aid in diagnosis. The value of the inoculation of guinea-pigs is considerably diminished by the necessary six weeks' delay. For these reasons we wish to emphasize the value of chemical analysis of the fluid, which can be completed within an hour after the lumbar puncture. This, taken with the pressure and cytologic observations, gives a picture of the cerebrospinal fluid which is of great importance in differential diagnosis.

Age.—Table 4 shows a comparison of the average values obtained for cerebrospinal fluid in infants, children and adults. No significant differences are noted.

29. Only tubes which have been thoroughly cleansed with "cleaning solution" should be used.

The cell count tends to be somewhat higher in adults than in infants and children, but the number of cases in the groups is too small to make such differences significant.

TABLE 4.—*Comparison of the Average Cerebrospinal Fluid Values in Infants, Children and Adults*

Ages	Number Patients (Total, 84)	Cells, per Cu.Mm.	Protein, Mg. 100 Cc.	Sugar, Mg. 100 Cc.	Chloride,* Mg. 100 Cc.
Under 4	18	156	188	22	618
4 to 14	13	196	152	31	567
Over 14	53	277	236	29	605
Average		243	220	28	604

* As sodium chloride.

TABLE 5.—*Determinations on Cerebrospinal Fluid in Five Cases in Which the Values Obtained at First Puncture Were Atypical*

Case	Age	Date	Initial Pressure, Mm. C.S.F.*	Cells, per Cu.Mm.	Protein, Mg. 100 Cc.	Sugar, Mg. 100 Cc.	Chloride,† Mg. 100 Cc.
18	35	6/30/29	380	...	200	48	682
		7/ 2/29	500	30	112	29	652
		7/ 3/29	500	47	92	36	641
		7/ 5/29	...	...	106	..	605
		7/ 6/29	...	...	128	5	486
		7/ 7/29	500	62	138	5	570
		7/ 8/29	500	113	160	5	553
		7/ 8/29	...	...	154	..	528
		7/10/29	...	...	160	5	570
		7/12/29	450	88	62	..	623
24	48	3/25/30	150	460	133	40	720
		3/26/30	430	320	200	42	702
		3/27/30	465	347	278	45	697
		3/28/30	...	452	364	40	697
		3/29/30	500	260	264	22	689
		3/30/30	400	560	264	28	666
		3/31/30	550	578	282	16	680
30	21	10/25/31	350	100	...	58	706
		10/26/31	360	211	75	53	684
		10/27/31	350	230	78	47	654
		10/28/31	360	240	98	33	645
		10/29/31	400	328	150	28	627
		10/31/31	800	450	51	..	584
		10/31/31	650	450	69	26	540
		11/ 4/31	650	480	138	45	553
48	18	8/26/26	...	98	122	49	722
		8/28/26	260	231	138	51	702
		8/30/26	320	467	130	46	643
		8/31/26	420	182	196	44	600
		9/ 1/26	420	74	114	47	600
		9/ 2/26	700	453	138	37	576
82	24	7/22/31	220	68	25	50	667
		7/24/31	240	120	57	54	654
		7/25/31	230	142	96	43	667
		7/26/31	230	95	114	36	649
		7/27/31	260	140	114	35	632
		7/28/31	260	155	90	32	627
		7/30/31	260	153	96	50	615
		8/ 1/31	300	...	114	36	622
		8/ 3/31	450	144	90	39	604

* Cerebrospinal fluid.
† As sodium chloride.

TYPICAL OBSERVATIONS

The typical fluid in tuberculous meningitis has the following characteristics:

1. The pressure is elevated (over 200 mm. of cerebrospinal fluid).

2. The appearance is clear or like ground glass, colorless or faintly xanthochromic, and the fluid usually shows a delicate weblike clot.

3. There is an increase in white cells (from 25 to 500 per cubic millimeter); lymphocytes predominate.

4. There is an increase in the protein content (from 45 to 500 mg. per hundred cubic centimeters).

5. The sugar level is decreased (below 45 mg. per hundred cubic centimeters).

6. The chloride content is decreased (below 650 mg. per hundred cubic centimeters).

7. The colloidal gold test shows a mild midzone reaction or no reaction.

ATYPICAL VALUES

If a puncture is done early in the disease the typical cerebrospinal fluid formula occasionally may be absent. Subsequent punctures will, however, nearly always show the typical changes. Table 5 shows the findings in 5 cases in which the puncture was done within a week of the onset of symptoms. The findings at the initial puncture were inconclusive. Later punctures, however, showed a progressive decrease in the sugar and chloride content, and the typical formula was soon present in all these cases. Exceptions to the complete formula may be found in any one or, rarely, in several of the tests.

Pressure.—The pressure was normal (less than 200 mm. of cerebrospinal fluid) in 11 of 61 cases in which it was measured at first puncture; in 8 of these punctures were done again, and in only 1 did the pressure fail to go above 200 mm. The pressure may occasionally be normal early in the disease, but nearly always becomes elevated on subsequent punctures.

Cells.—The cell count was less than 25 in 2 fluids and more than 500 in 25 of a total of 253 fluids. In case 67, 5 cells were found at the first puncture. Sugar, chloride and protein levels, however, were typical of tuberculous meningitis. Three and five days later the cell counts were 28 and 216, respectively, the cells being almost exclusively lymphocytes. In case 39, 10 cells were counted at the first puncture (the sugar and chloride again showing characteristic values). On the next day the cell count had increased to 29. Such instances of normal or slightly increased cell count at the onset, while rare, have been reported by several observers. Bickel [10] reported a case with no cells. Watts

and Viets [30] reviewed the literature and reported a case showing 4 lymphocytes at the first puncture, increasing to 205 lymphocytes six days later. Foord and Forsyth [16] reported 1 case showing 3 cells, increasing to 10 cells four days later. The sugar and chloride values were characteristically low. The finding of a low sugar value in such cases, with a normal cell count indicates that the decrease in sugar is not dependent on an increase in the number of cells. It should be remembered, therefore, that in exceptional cases the cell count may be normal at the onset, usually increasing within a few days. The determination of the protein, sugar and chloride content may make the diagnosis possible before the cell count has become elevated.

There was a preponderance of polymorphonuclear leukocytes in only 9 cases in which a differential count was made.

Protein.—The protein level was normal (less than 45 mg. per hundred cubic centimeters) in only 2, and more than 500 mg. in only 12 of 253 fluids. The extremely high values were usually encountered in cases in which a subarachnoid block had occurred. The lowest protein value in the lumbar fluid was 25 mg. in case 82 at the first puncture. At this time there were: an elevated pressure; a cell count of 68 per cubic millimeter (14 per cent polymorphonuclear leukocytes); sugar, 50 mg., and chlorides, 667 mg. per hundred cubic centimeters. The progressive changes in this case are presented in table 5. It will be seen that two days later the protein was 57 mg. per hundred cubic centimeters, and that the formula, atypical at the first puncture, soon became characteristic of the disease. Case 15, in which only one puncture was done, showed a protein level of 43 mg.; the chloride values were not determined; the pressure and sugar values were normal, and the cell count was 80 per cubic millimeter.

While either the cell count or the protein content occasionally may be normal, we have seen no fluid in which both these values were normal.

Sugar.—The sugar content was normal (50 mg. or over) in 17 of 222 lumbar fluids, the highest value being 59 mg. Cisternal fluid usually has a higher sugar value than lumbar fluid. One specimen of cisternal fluid, in a case showing subarachnoid block, had a value of 71 mg., while specimens of lumbar fluid drawn simultaneously showed 56 mg. (case 76). In case 32, fluid from three cisternal punctures showed a gradual fall from 60 to 45 mg. over a period of seven days. With rare exceptions the sugar value shows a progressive decrease as the disease advances (fig. 2 and table 5). In borderline cases a simultaneous estimation of blood sugar (taken after fasting if possible) is of great value, because moderate hyperglycemia may occasionally mask a falling

30. Watts, J. W., and Viets, H. R.: New England J. Med. **200**:757, 1929.

spinal fluid sugar value; for example, a spinal fluid sugar of 55 mg. is normal in the presence of a blood sugar of 100 mg. after fasting, but definitely low in the presence of a blood sugar of 180 mg. or higher.

Chlorides.—Chloride values of 700 mg. per hundred cubic centimeters or more have been seen in 7 instances, and values of 650 mg. or more in 45 of 202 fluids examined. In the 39 cases in which two or more punctures were done, fluids from 5 had values of 650 mg. or more at the last puncture. Fluids from 2 of the 54 cases failed to show a value below 650 mg. at some stage of the disease.

A progressive fall in the chloride level nearly always takes place (two exceptions, cases 6 and 57).

Colloidal Gold Curve.—There were 4 first zone curves and 16 end-zone curves in a total of 166 fluids. One of the first zone curves occurred in a patient with a positive Wassermann reaction in both blood and cerebrospinal fluid (tuberculous meningitis proved by autopsy and inoculation of guinea-pigs, case 19).

Wassermann Reaction.—The Wassermann test, performed in 60 cases, was positive in the cerebrospinal fluid in 2 cases (19 and 68), and doubtful in 1 (case 58). It was positive in the blood in only 1 of the 3 cases (19).

DIFFERENTIAL DIAGNOSIS

The complete formula for the cerebrospinal fluid in tuberculous meningitis is nearly pathognomonic of the disease. Our data show no appreciable difference in the fluids from infants, children and adults.

Yeast Meningitis.—This rare form of meningitis has reproduced the complete formula in the 2 cases we have seen (table 6). It can be distinguished from tuberculous meningitis only by finding the organism in smear or culture.

Acute Syphilitic Meningitis.—This may also simulate the typical formula and give real difficulty in differential diagnosis. Table 7 shows 3 such cases. In each of these the fluid corresponded to that of tuberculous meningitis, except that the Wassermann reaction of the spinal fluid was positive in each case. The Wassermann reaction is not always a safe criterion, however, because occasionally it may be negative in acute syphilitic meningitis. Moreover, it may be positive in tuberculous meningitis if the Wassermann reaction of the blood is positive or if the patient has syphilis of the central nervous system as well as tuberculous meningitis. The chloride values are helpful; in 40 fluids from 22 cases of acute syphilitic meningitis the average value was 691 mg. per hundred cubic centimeters. Six fluids showed a chloride level below 650 mg. (lowest value 636 mg.), while 17 fluids had values above 700 mg. Thus, chloride values of 620 mg. or less are a strong point against the diagnosis of acute syphilitic meningitis. Values of 650 mg. or

higher, however, are not strong evidence against the diagnosis of tuberculous meningitis, as such values occur not infrequently in that disease (in 45 of 202 fluids), especially at the onset. It is evident that the differential diagnosis between tuberculous meningitis and acute syphilitic meningitis may be extremely difficult to make. We have seen 1 case of syphilitic meningitis with a low sugar level in the cerebrospinal fluid (18 mg. per hundred cubic centimeters) and a cell count of 45 per cubic millimeter. The colloidal gold reaction is of some aid. A first zone

TABLE 6.—*Observations in Yeast Meningitis (Torula)**

Case	Initial Pressure, Mm. C.S.F.†	White Cells: Total	White Cells: Per Cent Polymorphonuclears	Protein	Sugar	Chloride	Colloidal Gold Curve	Wassermann Reaction
1	350	68	‡	190	39	579	22223320000	Doubtful§
2	210	120	78	137	38	619	0000255544	Doubtful‖

* The diagnosis was confirmed by cultures and at autopsy.
† Cerebrospinal fluid.
‡ The differential count was not made at this puncture. Three preceding counts showed 25, 38 and 51 per cent polymorphonuclear leukocytes.
§ The Wassermann reaction on a previous puncture was negative in one laboratory and positive in another.
‖ This patient had syphilis as well as yeast meningitis. The Wassermann reactions of both the blood and the spinal fluid were strongly positive on other dates.

TABLE 7.—*Determinations on Cerebrospinal Fluid in Three Cases of Acute Syphilitic Meningitis Which Yielded Values Closely Resembling Those of Tuberculous Meningitis*

Case	Initial Pressure, Mm. C.S.F.*	White Cells: Total	White Cells: Per Cent Polymorphonuclears	Protein, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Chloride, Mg. per 100 Cc.	Gold Curve	Wassermann Reaction
1	...	920	6	189	32	636	0011222221	Positive
2	300	282	0	114	26	649	5555555444	Positive
3	...	285	15	59	37	649	0012223210	Positive

* Cerebrospinal fluid.

curve occurred in 22 of 56 cases of acute syphilitic meningitis, while it occurred in only 4 of 84 cases of tuberculous meningitis, in 1 of which syphilis was present as well.

Acute Purulent Meningitis.—Meningitis due to the meningococcus, pneumococcus, streptococcus, staphylococcus, influenza bacillus or colon bacillus will rarely cause difficulty in differential diagnosis from tuberculous meningitis. The large number of cells, the predominance of polymorphonuclear leukocytes and the coarse clot serve to distinguish these fluids. The acute clinical course does not suggest tuberculous meningitis. Occasionally a low grade or chronic case of meningitis may

cause confusion, particularly if the cultures show no growth. Such cases may be difficult to distinguish from atypical cases of tuberculous meningitis.

Sugar determination is of no value in distinguishing tuberculous meningitis from acute purulent meningitis, as the sugar content is nearly always decreased in acute purulent meningitis. The chloride value is also lowered in acute purulent meningitis, although usually the decrease is less marked than in tuberculous meningitis. Values below 600 mg. per hundred cubic centimeters are distinctly more common in tuberculous meningitis than in acute purulent meningitis, while the reverse is true of values above 650 mg. Of 115 cases of acute purulent meningitis due to meningococcus, pneumococcus or streptococcus, 32 at some stage of the disease showed chloride values below 600 mg. per hundred cubic centimeters. It is evident, therefore, that chloride values below 600 mg. do not exclude the acute purulent forms of meningitis.

Lateral Sinus Thrombosis and Abscess of the Brain.—Both these conditions may give a low grade cellular reaction, increased pressure and a clinical picture not unlike tuberculous meningitis. The sugar value is normal or elevated in these cases unless there is a marked cellular reaction (1,000 cells or more), when a moderate decrease may occur, and the chloride value is normal or only slightly reduced except in cases complicated by high fever or by excessive vomiting. The predominance of polymorphonuclear leukocytes and the normal sugar value nearly always distinguish cases which might be confused clinically with tuberculous meningitis.

Tumor of the Brain.—An increase in the number of cells, which is not uncommon in tumor of the brain, may suggest tuberculous meningitis, but the normal sugar and chloride values rule out such a diagnosis, although when there has been excessive vomiting the chloride value may become decreased.

Acute Anterior Poliomyelitis.—This may be confused clinically with tuberculous meningitis, especially in the early stages. Moreover, the cerebrospinal fluids in these two conditions are superficially similar. In both the pressure may be elevated, a fine clot may form and a cellular increase, largely of lymphocytes, is the rule. The colloidal gold reaction is similar. The protein content is usually lower in poliomyelitis, especially in the early stages, but the real distinction is found in the sugar and chloride values. The sugar value is nearly always normal. In 124 fluids from 91 patients the sugar value was below 50 mg. in only 6, and below 45 mg. in only 1 case, in which the value was 41 mg. per hundred cubic centimeters. The average sugar value was 65 mg. The chloride values are most important. Of 99 fluids from 72 patients with acute anterior poliomyelitis, only 4 had values below 680 mg. and only

1 below 670 mg., this lowest value being 649 mg., while in tuberculous meningitis, as already noted, in the majority of cases the values lie below 650 mg. A sugar value below 50 mg. and a chloride value below 650 mg. are rarely found in poliomyelitis. They are the typical findings in tuberculous meningitis.

Epidemic Encephalitis.—This disease may resemble tuberculous meningitis clinically. The cerebrospinal fluid, however, is different. In epidemic encephalitis the pressure is nearly always normal; the cell count is usually less than 50 per cubic millimeter, and polymorphonuclear leukocytes are absent. The fluid is colorless and does not clot. The protein content is normal or, at most, moderately elevated. The sugar value is normal or elevated and the chloride value is normal. The cerebrospinal fluid in epidemic encephalitis cannot be confused with that in tuberculous meningitis provided an adequate examination is made.

Benign Lymphocytic Meningitis.—The clinical syndrome of benign lymphocytic meningitis is similar to that of tuberculous meningitis. The cerebrospinal fluid findings are also similar, with the exception of the sugar and chloride content. In benign lymphocytic meningitis the cerebrospinal fluid is under increased pressure, and shows a degree of lymphocytic pleocytosis and increased protein content similar to that found in tuberculous meningitis. The sugar content, however, is normal or increased, and the chloride content is normal or only slightly reduced.

Spinal Epidural Abscess.—This rare condition, usually due to Staphylococcus pyogenes-aureus, may show a fluid resembling that of tuberculous meningitis, with moderate cellular increase (mostly polymorphonuclears) and low sugar and chloride values; spinal subarachnoid block is nearly always present from the onset, while in tuberculous meningitis a block is usually a late complication.

Miscellaneous Conditions.—The following conditions occasionally may be associated with a moderate cellular reaction (usually lymphocytic) in the cerebrospinal fluid, and hence resemble tuberculous meningitis: postinfectious forms of encephalitis (measles, pertussis, scarlet fever) meningitis following mumps, herpes zoster, lead encephalopathy, cerebral softening (due to hemorrhage, thrombosis or embolus), acute transverse myelitis and Pott's disease. In all these conditions the sugar value is normal or elevated, and the chloride value is normal unless there has been high fever or excessive vomiting. Only rarely do these conditions simulate tuberculous meningitis clinically. A complete study of the cerebrospinal fluid will exclude the diagnosis of tuberculous meningitis in doubtful cases.

COMMENT

In tuberculous meningitis the cerebrospinal fluid undergoes certain modifications which are highly characteristic. The mechanism by which

these changes take place have been discussed in detail by Fremont-Smith.[27b] The pressure and appearance of the fluid, the cell content, the type of cell, the protein, sugar and chloride content, the colloidal gold curve and the Wassermann reaction form a cerebrospinal fluid syndrome of great diagnostic significance, far outweighing in value the information which can be obtained from any one or two of these tests.

Our data confirm the syndrome first described by Denigés and Sabrazés.[2] By means of the syndrome there is rarely any difficulty in distinguishing tuberculous meningitis from acute anterior poliomyelitis, epidemic encephalitis, abscess of the brain, lateral sinus thrombosis or acute purulent meningitis, whereas the clinical picture presented by these conditions is often impossible to distinguish from tuberculous meningitis, particularly at the onset. Acute syphilitic meningitis presents much greater difficulty in diagnosis; here the Wassermann reaction is of greatest help. Yeast meningitis can be distinguished from tuberculous meningitis only by identification of the organism in smear or culture. Fortunately this condition is rare.

Mestrezat [5] laid great emphasis on the cerebrospinal fluid chloride value in distinguishing tuberculous from other forms of meningitis. Combining his own data with those of others he assembled over 200 chloride determinations in 150 cases of tuberculous meningitis and over 300 determinations in 160 cases of acute nontuberculous meningitis. On the basis of these observations he stated: "A chloride value lower than 600 mg. per hundred cubic centimeters is always tuberculous in an acute meningitis." In Mestrezat's personal observations on 132 determinations in 68 patients, there were no exceptions to this rule, while in the literature he found only two exceptions which could be accepted as reliable (values of 595 and 570 mg. per hundred cubic centimeters). Greenfield and Carmichael [31] stated: "So far as we know such low readings (500 to 600 mg. per hundred cubic centimeters) are only found in tuberculous meningitis." They considered values below 580 mg. per hundred cubic centimeters as pathognomonic of tuberculous meningitis. Foord and Forsyth [16] took the same view.

As already indicated, our data provide many exceptions to these statements.

Meningococcic Meningitis.—In 8 of 50 cases the fluid before the intraspinal injection of serum showed chloride values below 600 mg. per hundred cubic centimeters; in 3 the values were below 580 mg., the lowest being 534 mg. Among 332 fluids from 59 cases after the intraspinal injection of serum, 65 fluids (18 cases) had values below 600 mg., 41 fluids (16 cases) having values below 580 mg.

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31. Greenfield, J. G., and Carmichael, E. A.: The Cerebrospinal Fluid in Clinical Diagnosis, New York, The Macmillan Company, 1925.

Pneumococcic Meningitis.—In the fluid from 7 of 31 cases (11 of 67 fluids) the values were below 600 mg. per hundred cubic centimeters. In 5 (7 fluids) the values were below 580, the lowest value being 486 mg.

Streptococcic Meningitis.—In the fluid from 17 of 32 cases (44 of 128 fluids) the values were below 600 mg. per hundred cubic centimeters. Ten of these (25 fluids) were 580 mg. and 3 (6 fluids) were below 580 mg., the lowest value being 477 mg.

Thus, in 115 cases of acute purulent meningitis due to the meningococcus, the pneumococcus or the streptococcus, in 32 (28 per cent), the cerebrospinal fluid chloride values were below 600 mg., while in 18 (16 per cent) the values were below 580 mg.

Mestrezat [5] also stated that a case of meningitis with a chloride value below 630 mg. at the first puncture practically always proves to be tuberculous. In 39 fluids obtained on the first puncture in nontuberculous meningitis he found only one value below 630 mg., while in the literature he found reports of only 2 fluids below this level. Our data do not confirm this statement. Among the cases cited, at first puncture, 20 cases of meningococcic meningitis showed chloride values below 630 mg. (8 below 600 mg.), 8 cases of pneumococcic meningitis, values below 630 mg. (2 below 600 mg.), and 17 cases of streptococcic meningitis, values below the level of 630 mg. (8 below 600 mg.).

In general we are in agreement with Mestrezat's findings with regard to the chloride values, but it is evident that there are many exceptions. A knowledge of the cerebrospinal fluid chloride value is of great diagnostic aid. It is, however, only one of the group of data which make up the cerebrospinal fluid syndrome. There is no chloride level which is pathognomonic of tuberculous meningitis or, as far as we know, of any disease.

Mestrezat [5] made the statement that in the absence of renal impairment (uremia): "A chloride value above or equal to 650 mg. per hundred cubic centimeters is never tuberculous." He found only one exception to this rule in his own cases (a value of 655 mg.) and only two exceptions in the literature (values of 655 and 660 mg.). Greenfield and Carmichael,[31] however, said: "In the earlier stages, readings between 680 and 700 mg. may be obtained." Foord and Forsyth [16] found values above 650 mg. in 7 of 65 fluids examined. In our series of 54 cases (202 fluids) with chloride determinations, 7 (45 fluids) showed values of 650 mg. or above, 7 fluids being 700 mg. or higher. In 2 of the cases with the chloride level above 650 mg. there were normal serum nonprotein nitrogen values. In case 79 the cerebrospinal fluid chloride values on four determinations ranged from 673 to 659 mg., the serum nonprotein nitrogen being 38 mg. In case 30 (table 5) an initial chloride value of 706 mg. was lowered to 684 mg. on the following day. At that

time the serum nonprotein nitrogen was 32 mg. In these 2 cases the chloride values above 650 mg. cannot be ascribed to renal impermeability (as far as this can be measured by the nonprotein nitrogen level in the blood). In 2 cases in which the cerebrospinal fluid chloride levels were above 650 mg., however, there were elevated blood or cerebrospinal fluid nonprotein nitrogen levels. In case 24 (table 5), which showed two chloride values above 700 mg., there was a cerebrospinal fluid nonprotein nitrogen value of 36 mg. (normal, from 12 to 28 mg.[26]). Case 6 (table 3) was particularly interesting. The cerebrospinal fluid chloride value climbed steadily from 635 to 732 mg., while the serum nonprotein nitrogen increased from 42 to 55 mg. In the other 13 cases showing chloride values of 650 mg. or higher, no determinations of the nonprotein nitrogen were made.

It may be said, then, that occasionally cerebrospinal fluid chloride values above 650 mg. may depend on renal damage as evidenced by retention of nitrogen, but such chloride values, especially early in the disease, in no way exclude the diagnosis of tuberculous meningitis.

It is evident that no hard and fast rules can be made for any single constituent in the cerebrospinal fluid. By grouping the data obtained from the several tests outlined, it is possible, however, to establish cerebrospinal fluid syndromes of diagnostic value for various diseases. The syndrome of tuberculous meningitis is highly characteristic.

CONCLUSIONS

The cerebrospinal fluid in tuberculous meningitis has a characteristic syndrome which rarely occurs in any other disease. The determination of the cerebrospinal fluid pressure, cytology, protein, sugar, colloidal gold reaction and Wassermann reaction is necessary to establish the syndrome.

VASOMOTOR DISTURBANCES RESULTING FROM CORTICAL LESIONS

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Circulatory disturbances accompanying hemiplegia have frequently been observed and recorded, but the functional significance of such vasomotor changes has not been sufficiently appreciated. Associated with the motor paresis which follows a lesion of the internal capsule or of the precentral cortex one often notes flushing and edema of the affected extremities accompanied by a change in the temperature of the skin. Many authors have attributed such changes to the peripheral concomitants of the motor paresis, but during the past eighty years an important body of evidence has accumulated which indicates that these vasomotor disturbances are actually cortical in origin.

REVIEW OF THE LITERATURE

In 1867 Chevallier [1] published a thesis entitled "De la paralysie des nerfs vasomoteurs dans l'hémiplégie." He said that Gubler in 1856 was the first to report a case of hemiplegia with associated changes in temperature. In 1863 Brown-Séquard reported a case of hemiplegia in which the temperature of the skin of the entire side of the body—of the ear and of the face as well as of the extremities—was higher on the affected than on the normal side. In all of Chevallier's cases the temperature of the skin of the paralyzed side was higher than that of the normal side; the difference in temperature varied, however, from 0.5 to 3.5 F., and the oral temperature showed diurnal variations of the same magnitude.

In 1886 Gowers [2] also described vasomotor and trophic changes in man following cortical lesions. Recently both Spiegel,[3] in 1928, and Brickner,[4] in 1930, gave comprehensive reviews of the literature concerning autonomic representation in the cerebral hemispheres, and in 1933 Olsen,[5] discussing temperature in relation

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1. Chevallier, P.-E.: De la paralysie des nerfs vaso-moteurs dans l'hémiplégie, Thèse de Paris, Paris, E. Martinet, 1867.

2. Gowers, W. R.: A Manual of Diseases of the Nervous System, London, J. & A. Churchill, Ltd., 1886, vol. 2, p. 77.

3. Spiegel, E. A.: Die Zentren des autonomen Nervensystems (Anatomie, Physiologie und topische Diagnostik), Berlin, Julius Springer, 1928.

4. Brickner, R. M.: Certain Characteristics of the Cortical Influence Over the Sympathetic Nervous System in Man, J. Nerv. & Ment. Dis. **71**:689 (June) 1930.

5. Olsen, A.: Hemiplegi og hudtemperatur, Hospitalstid. **76**:1097 (Nov. 9) 1933.

to infantile hemiplegia, cited many German and Scandinavian authors who had not been mentioned elsewhere in the literature.

The earliest experimental data appeared in the work of Eulenberg and Landois [6] in 1876. They reported alterations in the heterolateral temperature of the skin after stimulation of the postcentral region in dogs and in cats. François-Franck,[7] in 1887, recorded his own experimental evidence on the vasomotor changes produced by stimulation of the cortex in dogs, and Bechterew,[8] in 1911, concluded both from the work of other investigators and from his own experiments that cortical stimulation influences the pulse rate and the blood pressure as well as the temperature of the skin of the contralateral extremity. The changes in the galvanic reaction of the skin in response to cortical stimulation, as described by Langworthy and Richter [9] and by Wang and Lu,[10] give evidence of the influence of the cortex on sudomotor reactions.

In the course of an investigation on the effect of the extirpation of the motor and premotor areas on the motor performance of the monkey and the chimpanzee, it was observed that after ablation of the premotor area from one hemisphere the temperature of the skin of the opposite side of the body was lower than that of the normal side. This change always occurred, and although it was not permanent it invariably persisted long after the paresis had disappeared.

In order further to analyze this vasomotor phenomenon, the following experiments were carried out.

METHODS

Monkeys and chimpanzees were used, and the effect of the extirpation of various parts of the frontal and parietal lobes on the temperature of the skin was recorded by means of a Leeds-Northrop machine (Micromax) for the continuous recording of temperature. Sixteen monkeys were placed in a holding box, where they were restrained in a symmetrical position with both feet free and without restriction of the circulation. Under these conditions the temperatures of the skin were taken at corresponding points on the soles, and it was found that they were approximately the same for normal animals. Records taken of the temperatures of the hands and of the ears showed similar bilateral equality.

In the case of the chimpanzees the recording of continuous temperatures proved to be impossible, as this animal cannot readily be restrained or trained to remain

6. Eulenberg, A., and Landois, L.: Ueber die thermischen Wirkungen experimenteller Eingriffe am Nervensystem und ihre Beziehung zu den Gefässnerven, Virchows Arch. f. path. Anat. **68**:245, 1876.

7. François-Franck, C.-E.: Leçons sur les fonctions motrices du cerveau (réactions volontaires et organiques) et sur l'épilepsie cérébrale, Paris, Octave Doin, 1887.

8. von Bechterew, W.: Die Funktionen der Nervencentra, Jena, Gustav Fischer, 1911.

9. Langworthy, O. R., and Richter, C. P.: The Influence of Efferent Cerebral Pathways upon the Sympathetic Nervous System, Brain **53**:178 (July) 1930.

10. Wang, G. H., and Lu, T. W.: Galvanic Skin Reflex Induced in the Cat by Stimulation of the Motor Area of the Cerebral Cortex, Chinese J. Physiol. **4**:303 (Aug.) 1930.

in one position for a sufficient length of time. However, records taken at intervals showed changes which were consistent with those recorded for monkeys.

EXPERIMENTAL DATA

Vasomotor Changes.—After extirpation of the premotor area the temperature of the skin of the contralateral foot was found to be from 2 to 12 F. lower than that of the normal side. This change persisted in the chimpanzees for from three to six months and in the monkeys for from two to three weeks. On further analysis it was found that under

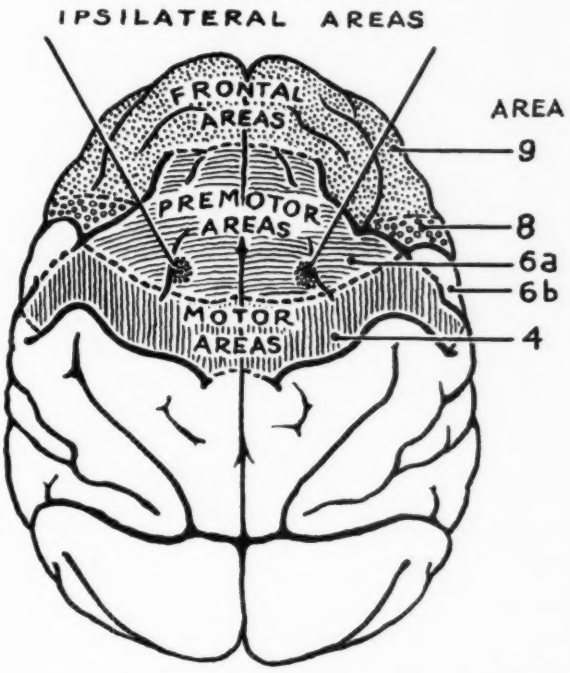

Fig. 1.—Cerebral hemispheres of a rhesus monkey showing the principal areas of the frontal lobes.

ordinary conditions of environmental temperature when the temperatures of the skin of the feet were low, i. e., when vasoconstriction was marked, a great difference usually existed between the temperatures of the two sides, but with vasodilatation (after struggling), when the temperatures of the feet were high, little or no difference was found.

In order to elucidate these differences the following procedure was developed.

The animals were placed in an incubator at a temperature of 90 F. (fig. 2) until vasodilatation was complete. This level of vasodilatation was from 2 to 4 degrees below the rectal temperature, which in a monkey at rest varies between

101 and 103 F. The monkeys were then transferred to a refrigerator at a temperature between 45 and 50 F. and kept there for twenty minutes. They were then returned to the incubator at 90 F.

Figure 2 shows that under these extremes of environmental temperature vasoconstriction and vasodilatation in the normal animal occur promptly and simultaneously in the two extremities. Following extirpation of the premotor area, however, a pronounced change in the rate of

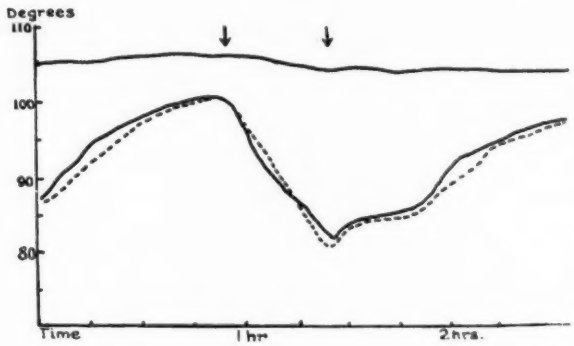

Fig. 2.—A normal temperature curve taken from the soles of the feet when the monkey was in an incubator at 90 F. The first arrow indicates the point at which the animal was placed in a temperature of 45 F., and the second arrow, the point at which the animal was replaced in the incubator. The top line shows the rectal temperature; the lower continuous line, the temperature of the left foot, and the lower broken line, the temperature of the right foot.

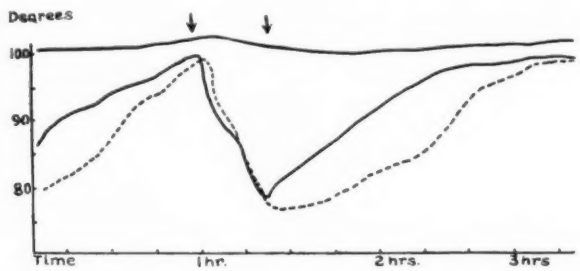

Fig. 3.—Temperature curves. The top line shows the rectal temperature of a monkey; the lower continuous line, the temperature of the normal left foot and the lower broken line, the temperature of the right foot after extirpation of the left premotor area and of the cortex. At the point indicated by the first arrow the animal was removed from the 90 F. temperature of an incubator to an environmental temperature of 45 F.; at the point indicated by the second arrow the animal was replaced in the incubator.

variation of the temperature of the skin was found in the affected extremities (fig. 3). Vasoconstriction occurred promptly and simultaneously in both lower extremities, *but vasodilatation occurred much*

more slowly in the affected limb. Ultimately, however, in every observation the temperature of the affected side rose to that of the normal side.

This lag in the rate of vasodilatation was clearly due to extirpation of the premotor area. No such changes resulted from extirpation of the frontal area or of the area posterior to the central sulcus. Extirpation of the motor area, however, led to a slight lowering of the temperature in the two animals in which this lesion was made. In two other animals in which the only operative procedure was the making of a slit between the motor and the premotor area, thereby dividing the fibers which pass from the premotor into the excitable motor region, the same slight drop in the temperature of the skin took place. This difference was increased by extirpation of the premotor area at a second operation. After the removal of an entire hemisphere in one animal changes in temperature were of the same type and magnitude as those which appeared after extirpation of the premotor area alone. In one animal a complete bilateral deafferentation of both lower extremities was effected, and subsequently the premotor area of one side was removed. This animal also showed a lag in vasodilatation on the affected side.

Sudomotor and Other Changes.—Other changes appeared in the affected extremities which were indicative of disturbances of the autonomic nervous system. The most striking of these was a pronounced diminution in the secretion of sweat, a phenomenon best seen after the injection of pilocarpine hydrochloride. Also, a transient edema of the hand and of the foot and some slight changes in color were sometimes observed. In one chimpanzee, which had been operated on six months previously, definite trophic changes were observed in the skin of the hand and of the foot. The blood pressure, the pulse rate and the pupillary and the pilomotor responses remained the same on the two sides.

COMMENT

Localization of the Cortical Area which Exerts an Autonomic Influence.—It is clear, then, that in the subhuman primates extirpation of the premotor area in the cortex alters the vasomotor control of the contralateral side of the body by disturbing the mechanism of reflex vasodilatation. Such a change cannot be attributed to alterations in the motor power of the extremities, since it is present after the paresis has disappeared and since it is absent or much less marked following lesions of the motor area in which the motor deficit is more profound. Also the temperature of the skin of the face and of the ear as well as of the palm and of the sole is changed.

The greatest difference in temperature is found when the premotor area of the cortex is removed, but extirpation of the motor area also causes slight changes in vasomotor response. This is probably due to the fact that fibers sweep caudally from the premotor to the motor

area before descending to the capsule, since a slit made in the gray matter between the two areas produces the same result.[11] Removal of the frontal, parietal, temporal or occipital areas causes no change in the temperature of the extremities.

Clinical evidence also suggests localization of the autonomic representation of the cortex in a region corresponding to the premotor area in the subhuman primates; thus, vasomotor changes in man as well as in the monkey are considered part of the syndrome of the premotor area,[12] which includes also forced grasping, spasticity and impairment of skilled movements. In the majority of human cases reported, the vasomotor changes are associated with spasticity, but changes in the temperature of the skin are not confined to the extremities. François-Franck[7] associated such changes with jacksonian attacks, and Olsen[5] found them in persons who had sustained injuries at birth. Olsen pointed out that although a motor deficit was present early in some of his patients, all of the symptoms except the vasomotor changes ultimately disappeared. Other autonomic changes have also been associated with this same area in man, such as an increase and a decrease in sweating in cases of hemiplegia. Brickner[4] reported two instances of pilomotor change associated with hemiplegia. In experimental animals Bechterew[8] found areas of the cortex which on stimulation produced alterations of the pulse rate, the pupillary response, salivation and the blood pressure, and Watts and Fulton[13] reported changes in the motility of the gastro-intestinal tract.

The postcentral sensory areas of the cortex have also been considered responsible for autonomic changes by observers who have reported alterations in the temperature of the skin in cases of hemiplegia in which sensation was affected. Langworthy and Richter[9] induced changes in the galvanic reaction of the skin from an area posterior to the motor area in cats. In the present series the removal of the postcentral convolutions in monkeys caused no change in the temperature of the skin, although in the same animals subsequent removal of the premotor area was followed by a characteristic fall.

Autonomic Tracts and the Effector Mechanisms Involved.—At the present stage of this investigation little can be added to the previous, rather indefinite, information concerning the course of the corticospinal

11. Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318 (Sept.) 1933.

12. Kennard, Margaret A.; Viets, H. R., and Fulton, J. F.: The Syndrome of the Premotor Cortex in Man: Impairment of Skilled Movements, Forced Grasping, Spasticity, and Vasomotor Disturbance, Brain **57**:69 (May) 1934.

13. Watts, J. W., and Fulton, J. F.: Intussusception—the Relation of the Cerebral Cortex to Intestinal Motility in the Monkey, New England J. Med. **210**: 883 (April 26) 1934.

autonomic pathways. Since somatic motor neurons arise in the motor and in the premotor region of the cortex, it is possible that neurons arising in the same region may also influence autonomic centers in the cord. The work of Langworthy and Richter [9] and of Spiegel and Hunsicker [14] indicated the possibility of direct corticospinal autonomic connections, but there is no reason to believe that autonomic impulses are actually carried by the somatic fibers. Langworthy and Richter produced increased sweating, as shown by the galvanic response of the skin, from points on the cortex and from the corticospinal and rubrospinal tracts in the cat. After section of the pyramidal tract in cats, Spiegel and Hunsicker succeeded in producing changes in temperature by cortical stimulation. They obtained similar results after section of the subcortical extrapyramidal projection systems, but when both the pyramidal and the extrapyramidal system were cut in the same animal no response could be obtained from stimulation of the cortex.

The efferent pathway concerned in the reflex disturbance would seem to pass by the anterior roots, since in the animal in which complete deafferentation of the lower extremities had been produced, subsequent extirpation of the premotor area was followed by a characteristic lag in the reflex vasodilatation. The effector fibers from the central nervous system which influenced this reflex, therefore, must run in the ventral motor roots.

Nature of the Autonomic Effects.—The nature of the cortical regulation of temperature cannot at present be elucidated. As somatic motor control from the cortex is regarded as being chiefly inhibitory,[15] so may pilomotor and sudomotor changes which occur after alteration of the cortical areas be due to the removal of inhibition. The thermal changes that are related to disturbances of the "heat-regulating centers" of the hypothalamus may be of the same nature, but whether the change in the rate of reflex vasodilatation which followed the procedures herein described was due to the cutting off of an active vasodilator mechanism or to the removal of an inhibitory influence on the mechanism of vasoconstriction has not as yet been determined.

CONCLUSIONS

1. In monkeys and apes after a lesion restricted to the premotor area of the cortex the temperature of the skin of the contralateral side of the body is lower than that of the normal side.

14. Spiegel, E. A., and Hunsicker, W. C., Jr.: The Conduction of Cortical Impulses to the Autonomic System, read at the Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 4, 1934; Proc. Soc. Exper. Biol. & Med. **31**:974, 1934.

15. Bard, P.: A Diencephalic Mechanism for the Expression of Rage with Special Reference to the Sympathetic Nervous System, Am. J. Physiol. **84**:490 (April) 1928.

2. This change is peculiar to lesions of the premotor area and does not occur after lesions of the frontal association, the occipital or the parietal area. A slight change of temperature follows the extirpation of the motor area alone.

3. This fall in temperature is due to an alteration in the mechanism for reflex vasodilatation, since a lag in the reflex vasodilatation is noted when the animal is subjected to a rise in environmental temperature, but the reflex vasoconstriction is prompt and normal following a drop in environmental temperature.

4. Other features related to the autonomic nervous system which are noted after extirpation of the premotor area of the cortex are transient edema, changes in the color of the skin and diminished production of sweat on the contralateral side of the body.

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ABSTRACT OF DISCUSSION

DR. PAUL C. BUCY, Chicago: This work, which demonstrates the representation of the autonomic nervous system in the cortex, is one of the most interesting and valuable contributions which have resulted from the investigation of the frontal lobe which is being carried on in Dr. Fulton's laboratory. Dr. Kennard is to be complimented on the ingenious methods devised for studying the vasoconstrictor and vasodilator reflexes in monkeys. Her study of the sympathetic vasomotor activity offers evidence that area 6, the premotor area, exercises an inhibitory control over the subcortical reflex activity of the somatic musculature. Area 6 seems to be the inhibitory area, as it were, of the cerebral cortex.

I recently had the good fortune to observe a patient practically at the onset of hemiplegia and to continue my observation for some time. In this particular instance, there were present all of the clinical manifestations of the complete removal from activity of one cerebral hemisphere, as though the lesion, temporarily at least, involved the entire internal capsule. A severe vasoconstrictor spasm involved the face and both extremities on one side. It continued for a few hours and then persisted in milder form for a few days. The entire phenomenon was of relatively short duration. I believe that this phenomenon has not been observed more commonly because it is transitory. The neurologist usually sees a hemiplegic patient for the first time several days, weeks, months or even years after the onset of hemiplegia. If it were possible to observe the patient at the time of the onset of the hemiplegia, I am sure that marked vasomotor changes would be noted in many cases. The other changes, such as those in sweating and in pilomotor activity, which have been described by Brickner and others, persist for a longer time after the onset and can be more readily demonstrated.

On the sole basis of clinical cases, there is no doubt that Dr. Kennard's observations are absolutely correct, and they clearly demonstrate the discrete localization of these functions in the cortex.

DR. THOMAS J. HELDT, Detroit: In considering the autonomic representation in the cerebral cortex, I suppose that this study may be regarded as dealing primarily with the preganglionic system of cells and fibers, or of their equivalents. What are the details of postganglionic expression, and how much consideration has been given to stimuli which are more complex than those mentioned? Refer-

ence has been made to electrical stimulation and to stimulation by drugs. How much of a study has been made of the more complicated sensory stimuli and the psychic factors that are so difficult to rule out and to separate at the time of stimulation by simpler methods?

I am wondering whether Dr. Kennard has given special study to such factors as might be involved when a securely leashed dog is presented with food that is just out of reach. Multiple stimuli are certainly at hand. To what extent is such a complex sensory stimulus comparable to electrical stimulation? This is probably a relative matter, but how much of a discount must be allowed for such relative and complex stimuli in the full explanation of the functions and the cerebral representations under consideration?

On the basis of the reflex arc response and the postganglionic innervation of viscera, what are the possibilities of a "short circuit," and how much "short-circuiting" is possible without actual central and precentral representation?

Dr. Margaret A. Kennard, New Haven, Conn.: There is one matter that I should like to bring up, namely, the point that was made as to the emotional factor in relation to temperature. In the monkey it was found that not only the skin temperature but the body temperature is greatly influenced by emotional factors. Since the rectal temperature varies 2, 3 and 4 F., depending on the state of excitement of the animal, that factor had to be taken into account in these experiments.

The usual procedure was to catch an animal and place it in a holding box. By the time it had been caught and put in the box its temperature was often two degrees higher than it was after it had remained quiet for an hour.

I think that the emotional factors must have something to do, of course, with the cortical influence on the mechanism which regulates the temperature of the skin, but I do not think that variations due to excitement influence the results here reported, because they were consistent time after time.

FRONTAL LOBE OF PRIMATES

RELATION OF CYTO-ARCHITECTURE TO FUNCTIONAL ACTIVITY

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CHICAGO

Recent studies on the functions of the cerebral hemispheres are of immediate importance to clinical medicine for the light they have shed on certain neurologic problems of general practice, such as the prognosis and interpretation of the symptoms in vascular hemiplegia, the basis of the gastro-intestinal and other vegetative disturbances accompanying lesions of the brain and the character of the mental impairment following the destruction of specific cortical areas. It is the purpose of this paper, and of the others presented at this symposium, to give a brief résumé of these studies and to point out the clinical implications.

At present few serious investigators deny the existence of cerebral localization, and a small number still insist on the sharp localization of specific functions in given portions of the brain. The central nervous system has come rather to be looked on as a highly integrated mechanism each cell of which has a demonstrable function to perform, not as an independent entity but as a unit essential for the successful operation of the mechanism as a whole. This newer point of view has arisen in large measure from the study of the finer cellular architecture of the cortex.

REVIEW OF THE LITERATURE

The existence of a physiologic localization of function was first clearly demonstrated by Fritsch and Hitzig's [1] discovery of the electrically excitable motor area and by Ferrier's [2] observation that specific paralyses followed the removal of these areas. The recognition of anatomic localization had its beginning when it was proved that the motor area gives rise to the corticospinal projection system. Further evidence of structural localization came from the study of the optic pro-

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From the Division of Neurology and Neurosurgery, University of Chicago Clinics.

Read as a part of a symposium on the functions of the cerebral cortex before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

1. (*a*) Fritsch, G. F., and Hitzig, E.: Ueber die elektrische Erregbarkeit des Grosshirns, Arch. f. Anat., Physiol. u. wissensch. Med. **37**:300, 1870; (*b*) Hitzig, E.: Untersuchungen über das Gehirn, Berlin, A. Hirschwald, 1874, vol. 16.

2. Ferrier, D.: Experimental Researches in Cerebral Physiology and Pathology, West. Riding Lunatic Asylum M. Rep., London **3**:30, 1893.

jection system (Henschen,[3] Brouwer and Zeeman,[4] Holmes,[5] Cushing,[6] Poljak,[7] and others), from that of the sensory projection system (Foerster,[8] Head[9] and Dusser de Barenne[10]) and from the study of aphasia and of the related phenomena (Head,[11] Meyer[12] and Marie[13]). More recent work on the premotor region indicated that skilled and specialized movements are also integrated in a specific cortical area (Vogt and Vogt,[14] Foerster,[8a] Fulton,[15] Jacobsen,[16] Kennard and Fulton[17] and Bucy and his co-workers[18]).

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3. Henschen, S. E.: On the Visual Path and Centre, Brain **16**:170, 1893.

4. Brouwer, B., and Zeeman, W. P. C.: Experimental Anatomical Investigation Concerning the Projection of the Retina on the Primary Optic Centers in Apes, J. Neurol. & Psychopath. **6**:1 (May) 1925; The Projection of the Retina in the Primary Optic Neuron in the Monkey, Brain **49**:1 (March) 1926.

5. Holmes, G.: Visual Localization and Orientation, Brit. M. J. **2**:826, 1917; Disturbances of Vision by Cerebral Lesions, Brit. J. Ophth. **2**:353, 1918; The Cortical Localization of Vision, Brit. M. J. **2**:193 (Aug. 16) 1919; A Contribution to the Cortical Representation of Vision, Brain **54**:470 (Dec.) 1931. Holmes, G., and Lister, W. T.: Disturbances of Vision from Cerebral Lesions with Special Reference to the Cortical Representation of the Macula, Brain **39**:34 (June) 1916.

6. Cushing, H.: Distortions of the Visual Fields in Cases of Brain Tumors: The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341 (Jan.) 1922.

7. Poljak, S.: The Main Afferent Fiber Systems of the Cerebral Cortex in Primates, Berkeley, Calif., University of California Press, 1932, p. 370.

8. Foerster, O.: (*a*) Die Leitungsbahnen des Schmerzgefühls und die chirurgische Behandlung der Schmerzzustände, Sonderbände z. Beitr. z. klin. Chir., 1927; (*b*) The Cerebral Cortex in Man, Lancet **2**:309 (Aug. 8) 1931.

9. Head, H.: Sensation and the Cerebral Cortex, Brain **41**:58 (Sept.) 1918. Head, H., and Holmes, G.: Sensory Disturbances from Cerebral Lesions, Brain **34**:102 (Nov.) 1911. Head, H., and Riddoch, G.: Sensory Disturbances in the Hand Following Injuries of the Cerebral Cortex, Brit. M. J. **2**:782 (Nov. 20) 1920.

10. Dusser de Barenne, J. G.: Experimental Researches on Sensory Loalisation in the Cerebral Cortex, J. Exper. Physiol. **9**:355, 1916; Experimentelle Untersuchungen über die Lokalisation des sensiblen Rindengebietes im Grosshirn des Affen (Macacus), Deutsche Ztschr. f. Nervenh. **83**:273, 1925.

11. Head, H.: Speech and Cerebral Localization, Brain **46**:355 (Nov.) 1923; Aphasia and Kindred Disorders of Speech, London, Cambridge University Press, 1926, vols. 1 and 2.

12. Meyer, A.: The Present Status of Aphasia and Apraxia, Harvey Lectures, 1909-1910, Philadelphia, J. B. Lippincott Company, 1911, p. 228.

13. Marie, P.: Revision de la question de l'aphasie, Semaine méd. **26**:241, 493 and 565, 1906. Marie, P., and Foix, C.: Les aphasies de guerre, Rev. neurol. **24**: 53, 1917.

14. Vogt, C., and Vogt, O.: Allgemeine Ergebnisse unserer Hirnforschung, J. f. Psychol. u. Neurol. **25**:273, 1919.

15. Fulton, J. F.: Forced Grasping and Groping in Relation to the Syndrome of the Premotor Area, Arch. Neurol. & Psychiat. **31**:221 (Feb.) 1934. Fulton, J. F., and Kennard, M. A.: A Study of Flaccid and Spastic Paralyses Produced by Lesions of the Cerebral Cortex in Primates, A. Research Nerv. & Ment. Dis., Proc. **13**:158 (Dec.) 1932.

(Footnotes continued on next page)

In the middle of the nineteenth century, Meynert [19] discovered that different portions of the cortex have a characteristic microscopic structure, but it was not until the discovery of the gigantopyramidal cells of the precentral cortex by Betz (1874 and 1881) [20] and the confirmation of this discovery by Bevan Lewis (1878 and 1880) [21] that the study of the cyto-architecture of the cortex really began. The first complete analysis of the cerebral cortex, with its division into distinct fields on the basis of the microscopic structure, was published by Campbell [22] in 1905. His studies were primarily concerned with the brain of man, of the orang-utan and of the chimpanzee. This important work was quickly followed by the outstanding studies of Brodmann,[23] who extended them to the brains of many other members of the animal kingdom. These classic investigations were further enlarged on by Mauss,[24] who studied the pattern of the myelinated fibers in various portions of the cortex, by von Economo and Koskinas,[25] whose extensive

16. Jacobsen, C. F.: Influence of Motor and Premotor Area Lesions upon the Retention of Skilled Movements in Monkeys and Chimpanzees, A. Research Nerv. & Ment. Dis., Proc. **13**:225 (Dec.) 1932.

17. Kennard, M. A., and Fulton, J. F.: The Localizing Significance of Spasticity, Reflex Grasping, and the Signs of Babinski and Rossolimo, Brain **56**:213 (July) 1933. Kennard, M. A.; Viets, H. R., and Fulton, J. F.: The Syndrome of the Premotor Cortex in Man: Impairment of Skilled Movements, Forced Grasping, Spasticity and Vasomotor Disturbances, ibid. **57**:69 (April) 1934.

18. Bucy, P. C.: (*a*) Electrical Excitability and Cyto-Architecture of the Premotor Cortex in Monkeys, Arch. Neurol. & Psychiat. **30**:1205 (Dec.) 1933; (*b*) The Relation of the Premotor Cortex to Motor Activity, J. Nerv. & Ment. Dis. **76**:621 (June) 1934. (*c*) Bucy, P. C., and Fulton, J. F.: Ipsilateral Representation in the Motor and Premotor Cortex of Monkeys, Brain **56**:318 (Sept.) 1933.

19. Meynert, T.: Neue Untersuchungen über die Grosshirnrinde und ihre örtlichen Verschiedenheiten, Vrtljschr. f. Psychiat., 1868; Med. Jahrb., Wien. **17**: 13, 1869.

20. Betz, W.: Anatomischer Nachweis zweier Gehirne, Centralbl. f. d. med. Wissensch. **12**:578 and 595, 1874; Ueber die feinere Structur der Gehirnrinde des Menschen, ibid. **19**:193, 1881.

21. Lewis, W. Bevan: On the Comparative Structure of the Cortex Cerebri, Brain **1**:79 (April) 1878; Researches on the Comparative Structure of the Cortex Cerebri, Phil. Tr. Roy. Soc. London (pt. 1) **171**:35, 1880. Lewis, W. Bevan, and Clarke, H.: The Cortical Lamination of the Motor Area of the Brain, Proc. Roy. Soc., London, s.B **27**:38, 1878.

22. Campbell, A. W.: Histological Studies on the Localisation of Cerebral Function, London, Cambridge University Press, 1905.

23. Brodmann, K.: (*a*) Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellbaues, Leipzig, Johann Ambrosius Barth, 1909; (*b*) Neue Ergebnisse über die vergleichende histologische Localisation der Grosshirnrinde mit besonderer Berücksichtigung des Stirnhirns, Anat. Anz. (supp.) **41**:157, 1912.

24. Mauss, T.: Die faserarchitektonische Gliederung des Cortex cerebri der anthropomorphen Affen, J. f. Psychol. u. Neurol. **18**:410, 1911.

25. von Economo, C., and Koskinas, G. N.: Die Cyto-Architektonik der Hirnrinde des erwachsenen Menschen, Vienna, Julius Springer, 1925.

atlas gives the most complete available study of the cytologic structure of the human cerebral cortex, by C. Vogt and O. Vogt,[14] who first attempted to correlate microscopic structure and the results of experimental physiologic studies, and by Foerster,[8a] who has abundantly confirmed in man what the Vogts found to be true in the monkey.

On the basis of these and other studies [26] an attempt will be made to describe the chief areas of the frontal lobes of certain of the more common primates and to correlate briefly the anatomic facts with recent physiologic observations.

CYTO-ARCHITECTURE OF THE FRONTAL LOBES

The frontal lobe in primates may be described simply as that portion of each cerebral hemisphere lying anterior to the fissure of Rolando and above the fissure of Sylvius. It is made up of two principal areas: the precentral area and the prefrontal or association area.

The Precentral Area (Motor and Premotor).—The precentral area is composed of two closely related cyto-architectonic fields, the true motor and the premotor area (areas 4 and 6 of Brodmann, fig. 1). Microscopically, the two are surprisingly alike, except for the fact that only in area 4 does one find the gigantopyramidal cells of Betz (fig. 2). The two areas are characterized by the presence of a relatively thin second layer, the external granular layer, and by the absence of the fourth or internal granular layer. The third and fifth layers, the external and internal pyramidal layers, respectively, are well developed, and it is in the internal pyramidal layer that the gigantic Betz cells are located. This overdevelopment of the pyramidal cells with the reduction in the cells of the granular layers is typical of an efferent or motor cortex. From the Betz cells originates the pyramidal tract,[27] the chief efferent pathway of voluntary motor activity. Because of this fact, area 4 is regarded as the origin of the "final common pathway" of the cerebral cortex, a pathway that becomes increasingly dominant over the lower centers as the phylogenetic scale is ascended. As evidence of the increasing importance of this tract may be cited the fact that the dog deprived of the pyramidal tracts behaves much as usual; even the entire cerebral cortex may be sacrificed without great interference with the movements of progression. Also the monkey, after a short period of adjustment, performs surprisingly well when deprived of these tracts, whereas in man, after the destruction of the pyramidal tracts, there is severe paralysis. It must be obvious, therefore, that the areas of the cortex

26. Bucy, P. C.: A Comparative Cyto-Architectonic Study of the Motor and Premotor Areas in the Primate Cortex, J. Comp. Neurol., to be published.

27. Holmes, G., and May, P.: On the Exact Origin of the Pyramidal Tracts in Man and Other Mammals, Brain **32**:1 (May) 1909.

of various species, however similar they may appear beneath the microscope, are not necessarily functionally equivalent. Experiments on monkeys and apes are useful in the evaluation of the physiologic processes in man, not because the functions of these animals are identical with those of men but because they are less dissimilar than are those of the lower forms.

Area 4 does not give rise to the only motor projection system of the cortex. Rostral to it lies another region higher in the neurologic

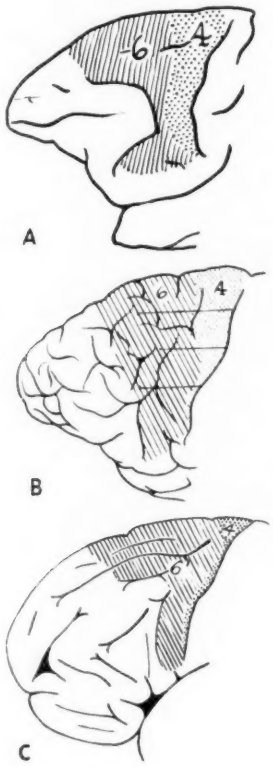

Fig. 1.—Schematic drawings of the frontal lobes of the brain of three primates: *A*, of the monkey (Macacus rhesus); *B*, of the chimpanzee and *C*, of man. The motor cortex (area 4) is indicated by stippling, and the premotor cortex (area 6) by cross-hatching; the frontal association area is plain.

hierarchy, the premotor area, or area 6. This area, lying immediately anterior to area 4 (fig. 1), has recently been shown to function as an integrator of voluntary motor activity and as a coordinator of postural adjustments (the extensive reflex muscular activities over which area 6 exercises control). Together, areas 4 and 6 give rise to the chief motor

projection systems of the cortex.[28] When these areas are absent the primate becomes a helpless organism, devoid of all volitional motor activity. Such a preparation is unable to sit, to stand, to walk, to eat or even to move of its own volition. Certain reflex muscular activities, freed from the inhibitory influence of area 6, remain. It is probable that certain movements of the eyes, effected through separate projection systems emanating from area 8 and possibly from area 9, immediately anterior to the precentral area, remain intact. For this reason area 8, at least in part, should probably be incorporated within the motor pre-

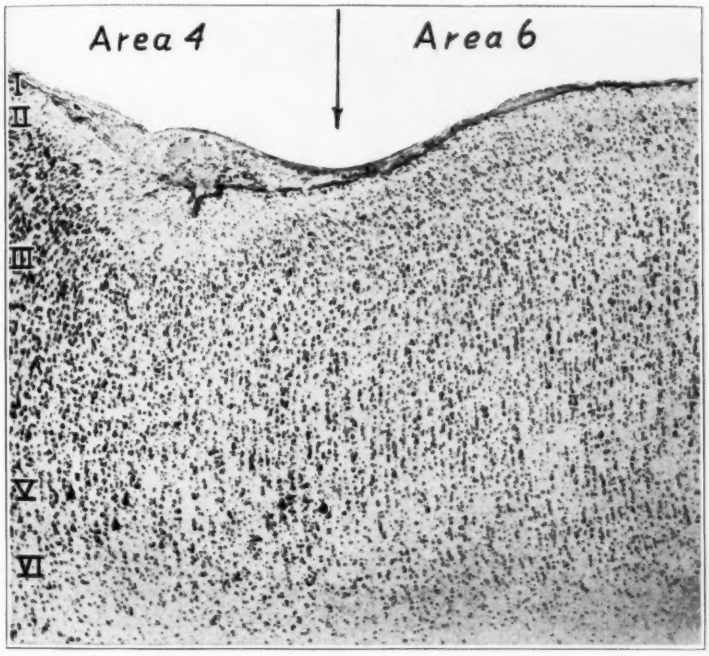

Fig. 2.—Photomicrograph of the precentral area (Macacus rhesus). The motor cortex, area 4, lies on the left of the arrow, and the premotor cortex, area 6, on the right. The external granular layer (*II*) is thin and the internal granular layer (*IV*) is absent, whereas the pyramidal layers (*III* and *V*) are prominent. The gigantopyramidal cells of Betz are present only in the true motor cortex.

central cortical field, but as yet the knowledge of its function is insufficient for definite classification. Area 6 is also concerned in the

28. Bieber, I., and Fulton, J. F.: The Relation of Forced Grasping and Groping to the Righting Reflexes: I. Preliminary Communication, Am. J. Physiol. **105**:7 (July) 1933. Bucy.[18b] Bucy and Fulton.[18c]

integration of reflexes involving the sympathetic nervous system;[29] it likewise influences subcortical centers involved in athetosis.[30]

The comparative development of the precentral cortical field in various primates is illustrated in the accompanying drawings of the frontal lobe of the common monkey (Macacus rhesus), of the chimpanzee and of man (fig. 1). It is to be observed that as the evolutionary scale is ascended area 4 gradually shrinks backward toward the rolandic fissure until in man it is almost entirely confined to the anterior wall of the central fissure except for the most superior portion of the leg area.

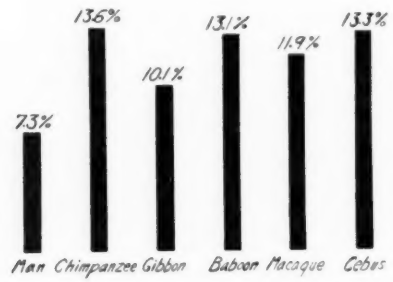

Fig. 3.—Graph prepared from data recorded by Brodmann,[23b] illustrating the relative extent of the precentral area (areas 4 and 6), expressed in percentage of the entire surface area of the cerebrum, in six species of primates.

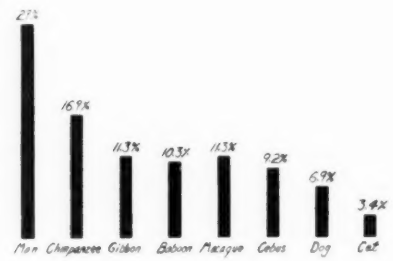

Fig. 4.—Graph prepared from data recorded by Brodmann,[23b] illustrating the relative extent of the prefrontal area (all of the frontal lobe except areas 4 and 6), expressed in percentage of the entire surface area of the cerebrum, in six species of primates.

Area 6, on the other hand, has changed little in its relation and position. The proportion of the entire cerebral cortex occupied by the motor field, the combined areas 4 and 6, is well shown in the graph in figure 3,

29. (*a*) Kennard, M. A.: Vasomotor Representation in the Cerebral Cortex, Science **79**:348 (April 13) 1934. (*b*) Watts, J. W., and Fulton, J. F.: Intussusception—the Relation of the Cerebral Cortex to Intestinal Motility in the Monkey, New England J. Med. **210**:883 (April 26) 1934.

30. Bucy, P. C., and Buchanan, D. N.: Athetosis, Brain **55**:479 (Dec.) 1932.

adapted from data found in the studies of Brodmann.[23b] It is true that, relative to the rest of the cortex, the motor area of man is smaller in extent than that of the other primates; however, this is due not to an actual decrease in the size of this area in the human brain but rather to a tremendous increase in the size of the remainder of the frontal lobe as shown in the graph in figure 4.

Frontal Association Area.—The prefrontal area constitutes practically all of the remainder of the frontal lobe. This lobe is composed

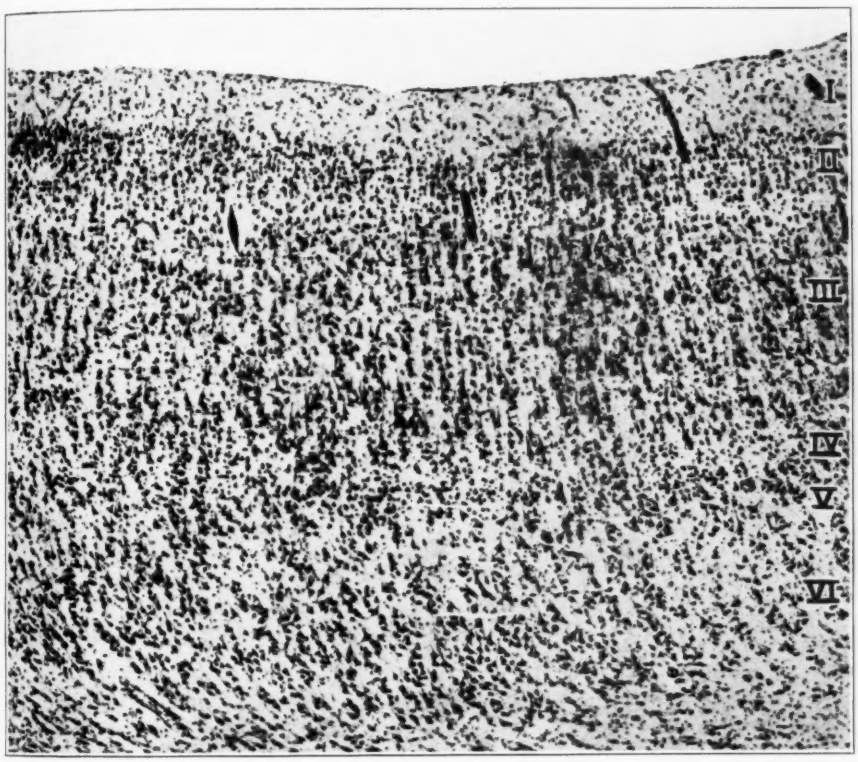

Fig. 5.—Photomicrograph of the cortex of the frontal association area (human). The external (*II*) and internal (*IV*) granular layers are much more developed in this area than in the precentral area, as seen in figure 2 (after von Economo and Koskinas).

of numerous areas, but all of them have certain microscopic characteristics in common. In contrast to the motor areas just described, the layers which were least developed or absent in the precentral area, that is, the granular layers, are well represented in the prefrontal, while the pyramidal layers which were prominent in the motor area are reduced in size in the frontal association area (fig. 5). The table and

figure 4 illustrate the great increase in the relative size of the prefrontal area in the higher apes and in man. This area has increased not only in proportionate size but in the complexity of the cyto-architectonic fields. This is illustrated by figure 6. The upper figure is a semi-schematic tracing of the cortex of the frontal lobe of the Old World monkey (Cercopithecus) after the Vogts.[14] The details do not differ essentially from the observations of Brodmann on the same species. The lower tracing of the human frontal lobe (fig. 6 *B*) is taken from Brodmann. Not only do all of the cyto-architectonic fields present in the monkey persist in man, but several new ones have appeared.

It is not to be anticipated that this enormous growth of the prefrontal area occurs unassociated with comparable changes in function. In the apes there is great increase in the dexterity of the extremities,

Surface Areas of the Prefrontal and Precentral Regions and Those of the Entire Cerebrum in Several Species of Mammals *

Mammal	Surface Area of Entire Cerebrum, Sq.Mm.	Surface of Prefrontal Area, Sq.Mm.	Ratio of Prefrontal to Entire Cerebral Area, per Cent	Surface of Precentral Area, Sq.Mm.	Ratio of Precentral to Entire Cerebral Area, per Cent
Man	135,470	39,287	29.0	9,889	7.3
Chimpanzee	39,572	6,719	16.9	5,381	13.6
Gibbon	16,302	1,839	11.3	1,646	10.1
Baboon	20,376	2,111	10.3	2,669	13.1
Macaque	15,308	1,733	11.3	1,821	11.9
Capushin (Cebus)	13,682	1,260	9.2	1,819	13.3
Dog	9,527	657	6.9		
Cat	4,474	152	3.4		

* Modification of the table and data of Brodmann.[23b]

as compared with that of lower vertebrate forms such as the carnivora, and associated with it is a tremendous development of that portion of the precentral area (area 6) concerned with the integration and coordination of the finer, more complex movements (table). In man the chief functional alteration from the apes is not in dexterity but in the utilization of that dexterity to build about himself a complex civilization. Is that utilization for the construction of a complex environment essentially correlated with the tremendous growth of the prefrontal area of man as compared with that of other primate forms? Many investigators are inclined to think so, though few assign such a development to this area alone, it being attributed rather to the increased complexity of the entire brain.

Except for that of the "eye" fields present in area 8 and possibly in area 9, knowledge of the specific functions of the various cyto-architectonic fields comprising the prefrontal lobe is inadequate. That

the functions possessed by this region differ widely from that of the integration of motor activity, the function of the motor or precentral area, is indicated by the dissimilarity in microscopic appearance of the two areas (figs. 2 and 5). The hypothesis has been advanced by numerous clinicians that the prefrontal region is primarily concerned with highly intellectual functions and social attributes.[31] The opinion is held, probably by a majority of neurologists, that the destruction of the prefrontal areas is associated with definitely demonstrable alterations in the intellectual capacities and personality. It is commonly thought that

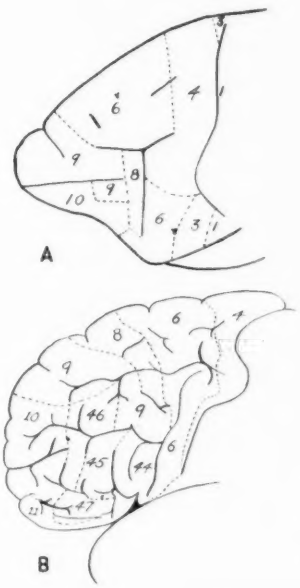

Fig. 6.—Schematic drawings of the cyto-architectonic fields of the frontal lobe (*A*) of the monkey (after the Vogts) and (*B*) of man (after Brodmann). An extensive development of the frontal association area has taken place in man as compared with the monkey, and the microscopic complexity of this area has greatly increased.

the absence of one of the prefrontal areas, the left in right-handed persons, is more productive of abnormal manifestations than is the

31. (*a*) Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 249. (*b*) Baruk, H.: Les troubles mentaux dans les tumeurs cérébrales, Paris, Gaston Doin & Cie, 1926. (*c*) Brickner, R. M.: An Interpretation of Frontal Lobe Function Based upon the Study of a Case of Partial Bilateral Human Frontal Lobectomy, A. Research Nerv. & Ment. Dis., Proc. **13**: 259 (Dec.) 1932.

absence of the other, but there is no unanimity of opinion on this point (Learmonth and Voris [32]).

COMMENT

The neuropathologist encounters great difficulties in estimating the extent of lesions of the frontal lobes, for such a lesion is generally a tumor, a cerebrovascular accident, embolism or thrombosis. Tumors are rarely confined to a single anatomic or physiologic area; they destroy function not alone by the destruction of tissue but by compressing it while pushing it aside and by obstructing blood supply. Tumors almost invariably confuse the picture by the general as well as by the local effect—by the increased intracranial pressure which stupifies and impairs the general attentiveness of the subject. Localized ischemia from thrombosis and embolism is rarely an isolated phenomenon. It occurs primarily in persons suffering from other diseases, such as syphilis, arterial hypertension, nephritis, myocardial insufficiency or generalized or cerebral vascular disease, all of which tend to produce widespread cerebral damage and make the accurate localization of a lesion and its correct correlation with the resulting symptomatology difficult and at times impossible. Nevertheless, there has grown up among neurologists the conviction that those intellectual and social defects so common in the presence of diffuse cerebral pathologic lesions are most typically the results of damage to the prefrontal area. This has been particularly well brought out by Brickner's [31e] recent study of a case in which the frontal association areas had been extirpated.

Since the experiments provided by nature on the complex prefrontal area of man are often too complex to clarify the problem, much concerning the prefrontal region must be learned from experimentation on the higher subhuman primates. It is true that the prefrontal area of the subhuman primates is vastly simpler than that of man, and the intellectual and social attributes of these animals are rudimentary. This, however, may prove a great advantage. In the present state of ignorance, simplicity is commendable. The brain of the monkey, of the chimpanzee and of the orang-utan may yet demonstrate the fundamental groundwork of the physiologic activity of the prefrontal area of man. Experimental psychologists have already made a beginning. With the realization that one is not dealing with human tissue—a lack of the perception of which marks so many pitfalls in the history of neurophysiology—with a detailed knowledge of the comparative structure of the brains of these primates as a guide and with the previous experience in experimentation on the primate cerebral cortex as a background, careful and painstaking work should be rewarded with the

32. Learmonth, J. R., and Voris, H. C.: Points in the Surgery of the Frontal Lobes of the Brain, Arch. Surg. **27**:506 (Sept.) 1933.

acquisition of newer and sounder data on which to build a correct and comprehensible neurophysiology of the human frontal lobe.

SUMMARY

The cellular structure of the frontal lobe of man and of the monkey is compared and correlated with the functional activities of its several regions. The relation of recent studies of cerebral localization to the problems of clinical medicine is also discussed.

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FUNCTIONS OF FRONTAL ASSOCIATION AREA IN PRIMATES

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Each frontal lobe, which consists of the tissue in the cerebral hemisphere lying anterior to the fissure of Rolando, may be divided into three major fields: the motor and the premotor area, already discussed by Bucy [1] and by Fulton and Viets [2] and the association area. The present communication concerns itself with the function of the association area; the terms "frontal association area," "frontal area" and "prefrontal area" are used interchangeably to designate that portion of the frontal lobe which lies anterior to the motor and the premotor area.

It is nearly one hundred years since misfortune befell Phineas Gage and gave to neurologic literature the famous "American crowbar case." The functions of the frontal area and the disturbances of behavior ensuing from lesions of this so-called "silent" area, have continued to interest both the clinical neurologist and the student of cerebral physiology. The Italian neurologist, Bianchi,[3] has summarized the defect following injury to the frontal area as a reduction in the capacity for "synthesizing" and for "serializing" groups of impressions without an obvious impairment of the capacity for receiving individual sensory impressions. The advances in modern surgical treatment of the brain have yielded clinical material of even greater value than have the earlier pathologic studies, since the longer survival of the patient makes possible the postoperative analysis of transient and residual deficits. The

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From the Laboratories of Comparative Psychobiology, Yale University School of Medicine.

Read as part of a symposium on the functions of the cerebral cortex before the Section on Nervous and Mental Diseases at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

Dr. J. F. Fulton and Dr. Margaret Kennard cooperated in the surgical work of the investigation, which has been a joint undertaking of the Laboratories of Physiology and of Comparative Psychobiology. A detailed report of the experiments on monkeys will be made in another journal; the results obtained in the experiments on chimpanzees will be reported by Jacobsen, Fulton and Wolfe.

1. Bucy, P. C.: Frontal Lobes of Primates; Relation of Cytoarchitecture to Functional Activity, Arch. Neurol. & Psychiat., this issue, p. 546.

2. Fulton, J. F., and Viets, H.: Upper Motor Neuron Lesions, Analysis of Syndromes of Motor and Premotor Areas, J. A. M. A. **104**:357 (Feb. 2) 1935.

3. Bianchi, L.: The Mechanism of the Brain and the Functions of the Frontal Lobes, translated by J. H. MacDonald, New York, William Wood & Company, 1922.

studies of Brickner,[4] Penfield and Evans,[5] German, Fox and their associates[6] and Spurling[7] paralleled in many essential details the experiments on monkeys and on chimpanzees.

Brickner,[4] in harmony with Bianchi's formulation, interpreted the fundamental disturbance of behavior associated with injury to the prefrontal area as a defect in synthesis; he indicated that although relatively simple material may be adequately synthesized, there exists a discernible, although not objectively defined, limit to the organization of behavior in a person whose prefrontal areas have been removed. It is my hope that the experimental analysis of the functions of the frontal lobe in the lower primates may throw further light on the nature of the disturbances of behavior and may indicate in more objective terms the conditions under which synthesis breaks down.

METHODS

Except for a characteristic restlessness, the behavior in the cage of a monkey that has undergone bilateral extirpation of the prefrontal area can scarcely be distinguished from that of an intact animal. Hence, in studying the more complex responses of animals it is necessary to supplement the usual observational technics with procedures for objective training. Since the tests have been described in detail elsewhere,[8] only the essential features will be indicated here.

Visual Discrimination.—In these tests, the animals learned to discriminate between: (*a*) a white and a black square; (*b*) two squares of different sizes, independently of the absolute size, and (*c*) various patterns, such as a square and a circle, a diamond and a triangle and a cross and a crescent.

Problem Boxes.—In order to obtain the food which had been concealed inside the problem box, the monkeys learned the manipulation of various locks, such as turning a crank, pulling ropes and levers, raising a handle and unfastening a hook.

Delayed Response.—In this test the animal observed the hiding of food under one of two identical cups; after a delay of a few seconds or of a few minutes it was allowed to choose one of the two test objects; if the selection was correct

4. Brickner, R. M.: An Interpretation of Frontal Lobe Function Based Upon the Study of a Case of Partial Bilateral Frontal Lobectomy, A. Research Nerv. & Ment. Dis., Proc. **13**:259, 1932.

5. Penfield, W., and Evans, J.: Functional Defects Produced by Cerebral Lobectomies, A. Research Nerv. & Ment. Dis., Proc. **13**:352, 1932.

6. German, W. G., and Fox, J. C.: Observations Following Unilateral Lobectomies, A. Research Nerv. & Ment. Dis., Proc. **13**:378, 1932.

7. Spurling, R. G.: Notes on the Functional Activity of the Prefrontal Lobes, South. M. J. **27**:4 (Jan.) 1934.

8. Jacobsen, C. F.: (*a*) A Study of Cerebral Function in Learning: The Frontal Lobes, J. Comp. Neurol. **52**:271 (April) 1931; (*b*) Influence of Motor and Premotor Area Lesions Upon the Retention of Skilled Movements in Monkeys and Chimpanzees, A. Research Nerv. & Ment. Dis., Proc. **13**:225, 1932. (*c*) Fulton, J. F.; Jacobsen, C. F., and Kennard, Margaret A.: A Note Concerning the Relation of the Frontal Lobes to Posture and Forced Grasping in Monkeys, Brain **55**:524, 1932.

it obtained the morsel of food, but if wrong, it was returned to the cage to wait the next trial.

For the purpose of later discussion it is desirable to emphasize certain characteristics of the tests. In the tests for visual discrimination and in the tests with the problem box, the essential cues which determine the animal's response are available in the subject's immediate environment at the time of the response; for example, the monkey can and does compare the two squares in the selection of the larger. But in the test of delayed response, immediate memory plays an important rôle, and it is necessary for the subject to recall the recent experience of seeing the food placed under one of the cups. Thus, while the sight of the cups may serve as a stimulus to recall the recent experience, it is not in itself adequate to give the differential cue necessary for a correct response.

EXPERIMENTAL RESULTS

Unilateral Lesions of the Prefrontal Area.—Unilateral lesions of the prefrontal cortex resulted in no impairment of the memory for the various tests which had been learned or of the ability to learn new problems. There was no evidence that either the right or the left frontal area was dominant over the other.

Bilateral Lesions of the Prefrontal Area.—Following bilateral lesions of the prefrontal area, either partial or complete, the results obtained differed in the two types of tests. After a complete bilateral extirpation the memory for the simple formed habits in the test with the problem box was unimpaired, and the ability to learn new habits of a similar nature was normal. Likewise, the adjustments to the tests for visual discrimination, whether they required discrimination on the basis of size, of form or of brightness, were not affected, and the animals lacking the prefrontal areas exhibited a normal ability to learn new visual discriminations.[8a] The tests of delayed response, however, revealed a profound deficit in what may be termed the recent or "immediate memory" (chart 1). Before operation the animal (frontal series, no. 5) scored a high percentage of correct responses after delays of fifteen, thirty and forty-five seconds. As the delays increased beyond one minute, however, the accuracy of performance decreased rapidly until after delays of one hundred and twenty seconds, the percentage of correct choices had no greater than a chance value. An inspection of chart 1 reveals that the complete removal of the frontal area on the left side did not impair the ability to execute the test of delayed response. However, the extirpation as well of the frontal association area of the opposite side permanently abolished the capacity for immediate memory, as measured by the test of delayed response. When placed in the testing cage, the animal observed with eagerness the loading of the food under one of the cups, and if it was permitted to seek the cup immediately, it made a correct choice in more than 90

per cent of the instances. However, if a delay as short as two seconds was interposed between the loading of the cups and the choice between them, the rate of accuracy of the response dropped to a value that might be obtained by chance. In a similar manner, when the animal responded to the loading of the cups without the introduction of delay, the momentary distraction of attention by incidental noises reduced the score to a mere chance value. It is significant that during the same periods in which the animal failed so completely in the test of delayed response, it skilfully manipulated the problem boxes and reacted with an accuracy of over 85 per cent to the tests for visual discrimination. Thus, the defect in the mechanism for delayed reaction cannot be regarded as a generalized deterioration of intelligence; it appears rather

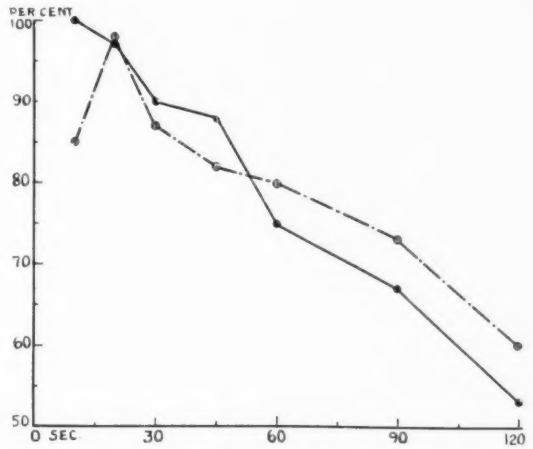

Chart 1.—Training record in tests of delayed response in a mangabey monkey, Cercocebus torquatus lunulatus (frontal series, no. 5), which underwent complete bilateral extirpation of the prefrontal area in two stages. In this chart and in the accompanying charts, the ordinates represent the percentage of correct choices; the abscissas, the length of the delay expressed in seconds. Likewise, the normal reactions of the preoperative period are indicated by a solid line with solid circles, and those following unilateral extirpation, by a broken line with circles and crosses. Complete failure to respond to the tests followed the bilateral extirpation.

to be a specific impairment of recent memory existing in the face of the normal adjustments made to other situations.

Partial Lesions of the Prefrontal Area.—The character of the deficit in memory is brought out more clearly by cases of incomplete lesions of the prefrontal area. In the preoperative tests (chart 2) the subject responded with a high degree of accuracy after delays of ninety seconds or less. As in the case of animal 5 of the frontal series, the extirpation

of one frontal lobe did not materially influence the performance; if anything, the monkey profited slightly from the additional training. The anterior portion of the remaining frontal association area was then excised, leaving intact a band of cortical tissue several millimeters in width lying anterior to the premotor area. In this instance the animal responded with a score of over 80 per cent after delays of from five to ten seconds, but it failed when the delays exceeded ten or fifteen seconds. There can be no question of the animal's ability to attend to the loading of the cups and to remember this experience for a short time. The retention of habits previously acquired with the problem box tests and the mastery of new tasks of a similar nature were not impaired by the lesion. During the eight months of postoperative

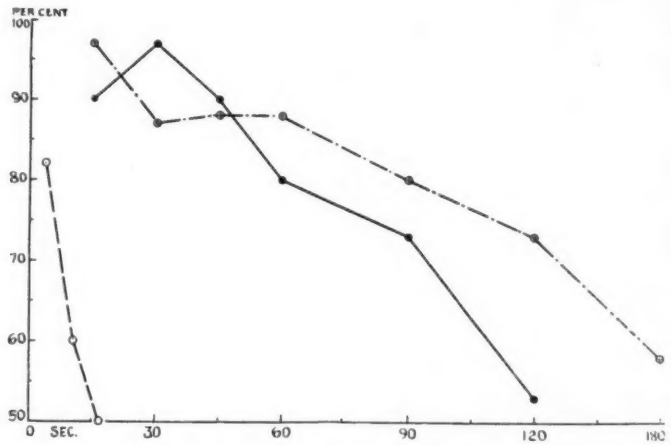

Chart 2.—Training record in tests of delayed response for a baboon, Papio papio (frontal series, no. 9), which underwent complete extirpation of the left prefrontal area and ablation of the anterior portion of the right prefrontal area. The broken line with hollow circles indicates the results obtained in the tests after the incomplete bilateral extirpation.

reeducation, more than forty times the number of trials which had been required to learn the problem in the preoperative training were given, but there was no significant improvement over the level of performance as it was measured one month after operation.

Lesions of Other Cortical Areas.—It is pertinent to inquire whether the defect in immediate memory is peculiar to lesions of the frontal association areas or whether it may also be found after injuries to other areas of the cortex. On this point the data are not as complete at the present time as might be desired, but it is significant that there have been no indications that lesions in other areas of the cortex abolish the

ability to perform the tests of delayed response. The areas which have been thus far investigated include the parietal association area, the premotor area and the temporal lobe. The results obtained from bilateral extirpation of the parietal association area are presented in chart 3 (frontal series, no. 8). If any difference is ascribed to the curves one is forced to conclude that the performance improved after bilateral extirpation of the parietal association area. This animal was subjected to further experimentation, and the frontal association area of the left side was subsequently removed. Although the test has not been completed, no impairment of the subject's ability to respond after delays of at least forty-five seconds is indicated. The interpretation that the disturbance of recent memory is peculiarly dependent on lesions of the frontal lobes

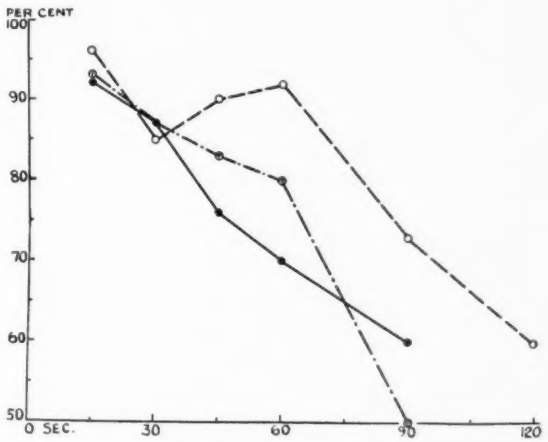

Chart 3.—Training record in the tests of delayed response for a mangabey monkey, Cercocebus torquatus lunulatus (frontal series, no. 8), which underwent bilateral extirpation of the parietal association area in two stages. The broken line with hollow circles represents the results of the test following the second operation.

is further supported by Breslau's [9] experiment on the postcentral gyrus which he removed bilaterally without the impairment of ability. The mass of cortical tissue involved in the animal (frontal series, no. 8) with extirpation of both parietal association areas and of one frontal area exceeded that in the animal with bilateral extirpation of the frontal lobe (frontal series, no. 5). Hence, the defect in behavior cannot be attributed merely to the extensive injury of the cortex. On the other

9. Breslau, B.; Barrera, S. E., and Warden, C. J.: The Effect of Removal of the Postcentral Convolution of the Macacus Rhesus Monkey upon Delayed Response, J. Comp. Psychol. **18**:207 (Oct.) 1934.

hand, the specificity of the frontal area is indicated in the mediation of the function which is measured by the test of delayed response.

COMMENT

It is evident from the foregoing material that bilateral lesions of the frontal association area modify certain aspects of the animal's behavior, while leaving intact the neural mechanisms requisite to its adjustment to other situations. The basic change associated with lesions of the prefrontal area is the loss of capacity for immediate or for recent memory. Hence it becomes pertinent to inquire whether a monkey without the prefrontal areas is capable of learning problems which, while not measuring immediate memory in the simple situation of the delayed response, depend on a capacity for immediate memory for their solution.

Jacobsen and Nissen [10] taught monkeys to open alternately a pair of doors in the training cage. Since the doors in themselves gave no differential cues on successive trials, it was necessary for the animal to remember which of the doors had been selected in the preceding trial. Bilateral extirpation of the frontal association area resulted in complete loss of this habit, and it is of even greater interest that in more than a thousand trials during postoperative training the problem was not relearned. This test illustrates another interesting aspect of the behavior of animals which have undergone the operation. The normal monkey in learning to respond to this situation readily became discouraged if it chanced to make as many as five or six successive errors, and even under the best of conditions it rarely made more than twenty or twenty-five trials per day. On the other hand, the animal which had been operated on performed as many as one hundred and fifty trials in a single period, in spite of the fact that it made frequent mistakes and that fifteen or twenty trials might be performed without a correct reaction. It seemed that the animal which had been operated on had little realization of the failures which before operation had disrupted the procedure of training.

Relation of Experimental and Clinical Studies.—The case of bilateral frontal lobectomy studied by Brickner [4] and his associates is particularly interesting because of the sharply marked surgical limitation of the lesion and because of the probable absence of complicating factors which usually mark the further growth of a neoplasm. Lack of restraint, as seen in the hostility of the patient toward his family and his friends, boastfulness, self-aggrandizement and distractibility characterized the patient during the postoperative period. The remote memory was less

10. Jacobsen, C. F., and Nissen, H. W.: The Influence of Frontal Lobe Lesions on the Delayed Alternation Habit, to be published.

impaired than was the memory for recent events, which was variable and faulty. There were indications that, although the learning of simple facts could be accomplished, the mastery of complex problems was difficult if not impossible. It was in the realm of the complex activities which are included under the terms reasoning, logical thinking and solving of problems that the intellectual defect showed itself most clearly. Spatial orientation was good, but orientation in time was faulty. Thus, the patient was disoriented as to the day of the week or of the month, and he had difficulty in remembering whether a given event had occurred a few days or several months previously, although the event itself could be recalled.

The fundamental deficiency in this case and in other cases of prefrontal lesions in man has been interpreted as a failure in synthesis, especially in synthesis of a more complex nature. But my associates and I in the experiments with the lower primates have shown that for such tasks as visual discrimination and the manipulation of the problem box both the memory and the ability to learn were normal. Hence it does not suffice to characterize the defect simply as a diminution of the capacity to learn or to synthesize, or to say that simple problems can be learned but that complex acts cannot be mastered, since in fact the impaired habits required less training than the responses which were retained. In the light of the results obtained from the experiments in delayed response, the description may be carried one step further. After an injury to the prefrontal areas those activities of the organism which in their very nature demand integration over a period of time cannot be carried out effectively. Temporal patterning fails because the subject can no longer remember a single experience for even a few seconds in the face of new incoming sensory data. The loss is not unlike that described by Bouman and Grünbaum [11] in their discussion of organic dementia—an inability to keep in mind a number of separate elements and at the same time to manipulate them in thought.

If allowance is made for the richer and more diversified nature of human behavior and primary consideration given to the functional equivalents in the adjustment to environment, the similarity between the deficiencies in behavior in man and those in the lower primates after prefrontal injury is indeed striking. To identify the processes of human thinking with those of delayed response in the monkey leaves one open to criticism; nevertheless it is pointed out that with the destruction of the frontal association areas a mechanism has been removed that is essential to the more complex forms of behavior, which are termed

11. Bouman, L., and Grünbaum, A. A.: Experimentell-psychologische Untersuchungen zur Aphasie und Paraphasie, Ztschr. f. d. ges. Neurol. u. Psychiat. **96**:481, 1925; cited by Lashley and Wiley.[12c]

logical thinking, judgment, and so on—that is, the capacity to organize the activity of the moment in terms of the immediate past experience. This ability seems to be peculiarly dependent on the intactness of the frontal areas.

Restitution of Function After Cortical Lesions.—The problem of the restitution of function after cortical lesions of greater or less severity is one of importance to the clinical neurologist as well as to the student of cerebral physiology. It has been recognized that after many cortical injuries a degree of functional recovery is possible, although, as Lashley [12] has pointed out, the mechanism of such a restitution is by no means clear. In the present experiment many times the amount of training required for preoperative learning was given the animals which had suffered complete bilateral lesion of the frontal association area, but there was no indication that they profited from the training. Harlow [13] studied the effects of the extension of the bilateral prefrontal lesions, produced by the periodic insertion of capsules of radon into the brain. The successively poorer performance in the tests of delayed reaction was correlated with the increasing size of the prefrontal lesion. In the cases in which the spread of the lesion was arrested before the complete abolition of function, more than a thousand trials for reeducation were given to the animal, but without significant improvement. Thus it seems likely that the extent of the lesion set a definite limit to the level of performance which was not altered by long and exhaustive training in the particular task. The course of recovery as noted in Brickner's patient is essentially in harmony with the results that we have obtained from extensive lesions in the monkey and the chimpanzee. With respect to the basic defects of behavior, Brickner's patient showed little improvement in the three or four years of postoperative life. He learned to make certain superficial adjustments to his social environment, but the basic defects, especially in the intellectual sphere, remained relatively unaltered.

The gradual but excellent recovery reported by Spurling [7] following unilateral lobectomy and the severe compression of the opposite prefrontal area stands in sharp contrast to that of the poorly oriented patient described by Brickner after a destructive bilateral lesion of the prefrontal area. It at once becomes apparent, both from the clinical and from the experimental data, that a degree of function is possible provided a cer-

12. Lashley, K. S.: (*a*) Integrative Functions of the Cerebral Cortex, Physiol. Rev. **13**:1 (Jan.) 1933; (*b*) Brain Mechanisms and Intelligence, Chicago, University of Chicago Press, 1929. (*c*) Lashley, K. S., and Wiley, L. E.: Studies of Cerebral Function in Learning: IX. Mass Action in Relation to Number of Elements in Problem to be Learned, J. Comp. Neurol. **57**:3 (Feb.) 1933.

13. Harlow, H. F.: Personal communication.

tain minimum of tissue of the frontal area remains intact but that a definite limit to the degree of function remains in spite of extensive reeducation after operation.

Equipotentiality of Cortical Areas.—A problem closely associated with the restitution of function and the limitation of recovery is the functional equipotentiality of different cortical areas. Lashley's [12] observations on the cortex of the rat clearly indicated that for certain problems a high degree of functional equivalence exists between the various cortical areas and that the extent of recovery bears a definite relation to the mass of intact cortical tissue, regardless of the locus of that tissue. It is apparent both from the experimental data obtained by my associates and me and from clinical observations that the widespread equipotentiality which Lashley found to operate in the rat does not exist in the brain of the primate. Thus, the delayed response could not be reacquired by animals after bilateral lesions of the frontal lobe, and in the case of partial lesions the degree of function could not be materially improved. This impairment, however, cannot be attributed to the mere destruction of cortical tissue, since even larger lesions of other parts of the cortex were made without the disturbance of the functions which are disrupted by lesions of the frontal area. It seems probable that between the functional activity of the brain of the rodent and that of the primate a further specialization has taken place, not only in the sensory and motor fields, as has been recognized, but in the associative functions of the organism. It would be erroneous, however, to leave the impression that the principle of mass action does not apply to the brain of the primate. No indication has been noted that a particular region of the frontal association area is necessary to the execution of these functions, and the available evidence suggests that the degree of the deficit is related to the amount of intact tissue of the frontal lobes. It is possible to harmonize the two divergent views, that of specificity on the one hand and of equipotentiality on the other, by the recognition of the principle, advanced by Poljak [14] and by Lashley,[12b] of areal equipotentiality.

SUMMARY AND CONCLUSIONS

The rôle of the frontal association areas in the mediation of complex behavior has been studied in the lower primates. Monkeys and chimpanzees were trained by several types of behavior tests: First, situations in which the essential cues were available in the subject's environment at the time of response, and second, situations in which

14. Poljak, S.: The Main Afferent Fiber Systems of the Cerebral Cortex in Primates, Univ. Calif. Publ. Anat., vol. 2, Berkeley, Calif., University of California Press, 1932.

the essential cues had to be recalled from recent experience. Experimental lesions were then made in various areas of the cerebral cortex, and the ensuing disturbances of behavior were analyzed.

The following conclusions are drawn from the study:

1. Unilateral lesions of the frontal association area (prefrontal area) resulted in no impairment of performance in any of the tests. There was no evidence of hemispherial dominance.

2. Bilateral prefrontal lesions, either partial or complete, produced different results with the two types of tests. Memory for the habits acquired with the problem box and for the visual discriminations based on size, form or brightness was not impaired, nor was there reduction of the ability to learn new tasks of a similar nature (tests of type 1).

On the other hand, tests which depended on recent memory (tests of type 2) revealed profound deficits. Thus, after complete bilateral lesions, there was severe impairment of recent or of immediate memory after delays as short as two seconds. Incomplete bilateral lesions resulted in shortening of the length of time through which recent memory was effective, but they did not entirely abolish this capacity. The defect in memory cannot be regarded as a generalized deterioration of intelligence but appears to be a specific impairment of recent memory existing in face of the normal adjustments made to other situations.

3. The defect of recent memory cannot be attributed merely to an extensive injury to the cortex, since lesions to other areas produced minimal, if any, changes; on the other hand, the specificity of the frontal area in the mediation of this function is indicated.

4. The fundamental deficiency in cases of bilateral prefrontal injury in man has been interpreted as one of failure in synthesis. Observations on the lower primates suggest that this failure in synthesis and in temporal patterning of behavior is due to a defect of immediate memory.

5. Extensive reeducation after operation failed to reestablish the capacity for immediate memory in animals with complete lesions, and it did not materially improve the performance after partial lesions.

6. The experiments indicate a high degree of specialization in the associative functions of the cortex in primates in contrast to the widespread equipotentiality which has been shown to operate in the cortex of the lower animals.

333 Cedar Street.

ABSTRACT OF DISCUSSION

On Papers of Drs. Bucy and Jacobsen

Dr. T. Diller, Pittsburgh: Reference has been made in this symposium to the famous crowbar case, which occurred one hundred years ago. It was a remarkable case. Ever since that time students have wondered about the frontal lobes. It is said that there are no silent areas in the frontal lobes, with which I agree.

I see considerable clinical difficulty which must be faced by these investigators. In cases of organic lesions in various parts of the brain other than the frontal lobes, mental symptoms may arise. With all of the light that is shed today on the function of the frontal lobes, clarity is still lacking. The confusion which may arise from mental symptoms due to disturbances in other parts of the brain must be borne in mind. Although the material that has been presented here is commendable, it should not be thought that much is known of the frontal lobes.

Dr. A. L. Skoog, Kansas City, Mo.: I should like to ask Dr. Bucy one question. He presented a slide on the screen showing the brain of the monkey and of man in which the frontal and prefrontal areas were blocked out in a large number of small areas, numbered specifically. He gave physiologic data relative to some of these areas, but none on many of the others. The question arises whether the areas really represent cleancut physiologic territories as Dr. Bucy suggested. I question whether they can be too closely implied in clinical psychiatric practice.

Dr. Henry R. Viets, Boston: Dr. Bucy's note regarding the localizing value of forced grasping is, of course, of great importance to clinical neurologists. I think the point should be made that unilateral forced grasping has marked localizing significance, whereas bilateral forced grasping has much less. As Dr. Bucy has pointed out, general intracranial pressure may give rise to bilateral forced grasping and may not indicate a primary lesion of the premotor area.

Dr. Walker Freeman, Washington, D. C.: I hope that Dr. Bucy's previous work on forced grasping resulting from lesions in other locations in the brain will not come back to plague him. It is my opinion that in cases of many acute lesions of the brain this phenomenon can be elicited but that in the chronic preparations forced grasping is characteristic of lesions in the premotor area or in its underlying tissues.

Dr. C. F. Jacobson, New Haven, Conn.: In reply to Dr. Diller's question I wish to say that I agree with him that mental disturbances may result from lesions of other portions of the cortex.

The point in which I was particularly interested was the patterning of the defects which are associated particularly with the frontal area. It is also possible that mental disturbances may be found in cases of lesions in other portions of the cortex and may be due to secondary factors, such as increased pressure.

Dr. Paul C. Bucy, Chicago: Dr. Freeman spoke of the two cases of forced grasping associated with lesions outside of the frontal lobes which I reported a few years ago. Both of the cases were of tumors, and in both bilateral forced grasping was manifested. These cases are not arguments against the origin of forced grasping from lesions of area 6; they merely point out that in cases of increased intracranial pressure forced grasping, especially when bilateral, is of little localizing significance.

Dr. Skoog asked concerning the physiologic significance of the numerous cytoarchitectonic fields of the human frontal lobe. These fields are purely anatomic and are localized by means of microscopic examination. The physiologic significance of most of them is as yet unknown.

HYPOTHERMIA IN CASES OF HYPOTHALAMIC LESIONS

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AND
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The extensive anatomic and physiologic investigations of the hypophysis and of the nuclear masses of the hypothalamic region in cases of polyuria, polydipsia, adiposity and genital dystrophy are fairly conclusive. Most observers agree that these symptoms are caused by lesions of the hypothalamic nuclei or of their pathways which are in direct communication with the hypophysis.

The exact localization of the center for the regulation of body temperature is still doubtful. A number of clinical and experimental facts seem to indicate that the nuclei in the walls of the third ventricle are concerned with heat regulation. These observations, however, were concerned not with the abnormal loss of heat but with the abnormal production of heat, i. e., hyperpyrexia. The subnormal temperatures described as occurring in cases of tumor, as in cases of craniopharyngioma or of lesions about the tuber cinereum, were not much below 97 F. The more marked reductions of temperature noticed following operations in the region of the tuber cinereum were of short duration and usually lasted for from twenty-four to forty-eight hours.

The case to be described is unique in that, in addition to marked and persistent hypothermia, there were also present the usual symptoms and signs of hypothalamic involvement (polyuria, polydipsia, adiposity and somnolence). The neoplasm, situated in the floor of the third ventricle, was limited in its destructive process to the vegetative nuclei of the tuber. Prolonged subnormal temperature of the degree present in this case has not, so far as could be determined, been recorded in the literature.

ANATOMY OF THE HYPOTHALAMIC VEGETATIVE NUCLEI

For purposes of orientation in the description of the sections of the hypothalamic region, which in this case were cut serially, it is advisable to enumerate briefly the nuclear masses and pathways of the region of

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From the Neuropathological Laboratory and Neurological Division, Montefiore Hospital.

Read at the Sixtieth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 5, 1934.

the tuber cinereum. Greving's [1] and Malone's [2] classifications were adopted for this purpose. For a more detailed study the reader is referred to the writings of these authors. The nuclei on each side are divided into two groups:

I. The cell groups in the diencephalic region and the wall of the third ventricle (fig. 1*A*):

1. Nucleus supra-opticus
2. Nucleus paraventricularis
3. Nuclei tuberis
4. Nucleus mamillo-infundibularis
5. Nucleus pallido-infundibularis
6. Nucleus interfornicatus
7. Substantia grisea centralis

II. The cell groups in the region of the mamillary body (fig. 1*B*):

1. The nuclei of the mamillary body, consisting of the nucleus magnocellularis, nucleus parvocellularis and nucleus mamillaris cinereus
2. Nucleus intercalatus
3. Nuclei of the wall of the third ventricle
   (*a*) Nucleus paraventricularis
   (*b*) Nucleus reuniens
   (*c*) Nucleus paramedianus
4. Substantia grisea centralis

The supra-optic nucleus (fig. 1*A*) extends from the anterior perforated space as far back as the optic tract, lying dorsolaterally and medially to it. The nerve cells are polygonal and contain coarse processes; the Nissl substance, in the form of large masses, is collected at the periphery of the cells.

The paraventricular nucleus (fig. 1*A*) lies close to the lateral wall of the third ventricle between the anterior commissure and the optic chiasm. The nerve cells differ little from those of the supra-optic nucleus. The Nissl substance of these ganglion cells collects in smaller masses and is scattered throughout the cytoplasm instead of at the periphery only.

The nuclei of the tuber situated in the floor of the third ventricle, consist of several groups of cells (fig. 1*A*). They extend from the caudal end of the optic chiasm to the anterior part of the mamillary body.

1. Greving, R.: Zur Anatomie, Physiologie und Pathologie der vegetativen Zentren im Zwischenhirn, Ergebn. d. Anat. u. Entwcklnsgesch. **24**:348, 1923. Greving, R., in Müller, L. R.: Lebensnerven und Lebenstriebe, ed. 3, Berlin, Julius Springer, 1931.

2. Malone, E. F.: The Nuclei Tuberis Lateralis and the So-Called Ganglion Opticum Basale, Johns Hopkins Hosp. Rep., no. 6, 1914.

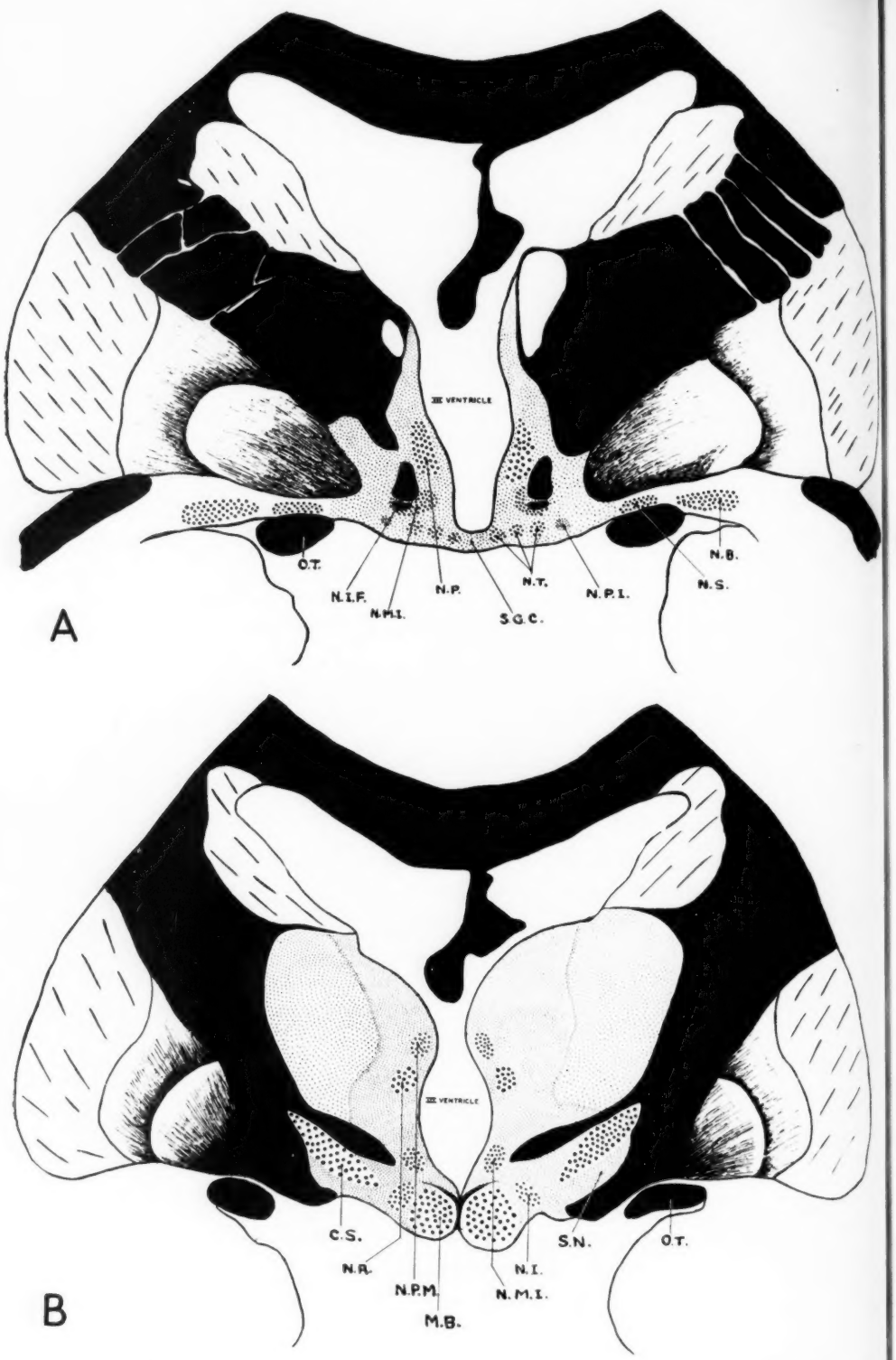

Fig. 1.—*A* shows the hypothalamic groups of nerve cells in a section through the middle of the third ventricle; *B*, the hypothalamic groups of nerve cells in a section through the anterior third of the mamillary bodies (modified after Greving). In these diagrams, *O.T.* represents the optic tract; *N.I.F.*, the nucleus interfornicatus; *N.M.I.*, the nucleus mamillo-infundibularis; *N.P.*, the nucleus paraventricularis; *N.T.*, the nuclei tuberis; *S.G.C.*, the substantia grisea centralis; *N.P.I.*, the nucleus pallido-infundibularis; *N.S.*, the nucleus supra-opticus; *N.B.*, the nucleus basilis; *C.S.*, the corpus subthalamicus (Luysii); *N.R.*, the nucleus reuniens; *N.P.M.*, the nucleus paramedianus; *M.B.*, the mamillary body; *S.N.*, the substantia nigra, and *N.I.*, the nucleus intercalatus.

The nerve cells are smaller than those of the supra-optic and paraventricular nuclei; they have a relatively small nucleus with a large amount of cytoplasm. The Nissl substance, in the form of small granules, is evenly distributed throughout the cytoplasm.

The substantia grisea centralis extends from the thalamus to the floor of the third ventricle and from the optic chiasm to the mamillary body and, without a sharp line of demarcation, passes into the substantia grisea centralis of the midbrain. Most of the nerve cells, which are small and have a relatively large nucleus, contain a small amount of cytoplasm, fairly coarse granules and small masses of Nissl substance which are scattered throughout the cytoplasm. There are also larger cells which are more numerous in an area ventral to the fornix.

The mamillo-infundibular nucleus (fig. 1*A* and *B*) consists of a group of cells in the posterior half of the third ventricle and is situated ventrally and dorsally to the nuclei of the tuber and to the mamillary body. The nerve cells are for the most part round and at times triangular, without a clear cell membrane. The nuclei are round and are generally located at the periphery. The Nissl granules are irregularly distributed and are aggregated in larger masses at the periphery of the cells.

The pallido-infundibular nucleus is situated in the middle part of the tuber cinereum between the nuclei of the tuber and the optic tract (fig. 1*A*). The nerve cells are differentiated with difficulty in Nissl preparations; in silver preparations they consist of large elongated cells with long processes.

The interfornicate nucleus is located between the fibers of the columna fornicis (fig. 1*A*). The nerve cells are best seen in silver preparations; they are essentially bipolar and elongated and have long processes.

The nuclei of the mamillary body (fig. 1*B*) are formed by the nucleus magnocellularis, nucleus parvocellularis and nucleus mamillaris cinereus. The nucleus magnocellularis lies medially. The nerve cells are multipolar, with three or four processes; the nuclei are round and large with a distinct nuclear membrane and are surrounded by little cytoplasm. The Nissl substance, consisting of dustlike, fine granules, is evenly distributed. The nerve cells of the nucleus parvocellularis are smaller; otherwise they have the same type of structure as those of the nucleus magnocellularis. The nucleus mamillaris cinereus is situated ventrally and laterally. The nerve cells cannot be distinguished easily in Nissl preparations. In silver preparations they are club-shaped with a long process which divides into many branches.

The intercalate nucleus lies laterally to the mamillary body (fig. 1*B*). The nerve cells, multipolar and elongated, are similar to those of the hypoglossal nucleus. They contain an oval, lightly stained nucleus and

a large cell body without a definite limiting cell membrane. Dustlike Nissl granules are diffusely scattered throughout the cell body; larger Nissl granules, resembling those of the cells of the anterior horn, are also seen.

The nucleus reuniens is situated in the massa intermedia and extends into the thalamus (fig. 1*B*). The nerve cells have a large, round nucleus with an indistinct nuclear membrane surrounded by little cytoplasm. The protoplasm of the cells consists of dustlike Nissl granules intermixed with single larger granules.

The paramedian nucleus lies dorsally to the nucleus reuniens near the third ventricle (fig. 1*B*). The nerve cells are like those of the dorsal vagus nucleus and the vegetative cells of the lateral horn. They are small, unipolar or bipolar and have a large, oval nucleus with an indefinite nuclear membrane and a small amount of protoplasm. The cytoplasm consists of fine, dustlike as well as coarser granules.

Pathways of the Hypothalamic Nuclei.—The hypothalamus has connections with the frontal lobes, olfactory system, thalamus, spinal cord (?) and pituitary gland. For this presentation it will be necessary to review only the pathways to the hypophysis. The best known tract is the tractus supra-opticus hypophyseus, which extends from the nucleus supra-opticus via the infundibulum to the hypophysis. The tractus paraventricularis cinereus has its origin in the nucleus paraventricularis and ends near the nucleus supra-opticus. Whether its fibers terminate in the nucleus supra-opticus or join the tractus supra-opticus hypophyseus, finally reaching the hypophysis, has not yet been determined.

REPORT OF A CASE

History.—M. R., a single man, aged 31, Jewish, born in Russia, was admitted to the Montefiore Hospital on Jan. 5, 1933. He had been well until 11 years of age, when bilateral progressive loss of vision developed. This condition necessitated attendance at a school for the blind for about one year, when, without medical intervention, vision gradually improved. He remained well for seven years, until 1921, when anorexia, polydipsia and polyuria appeared. Following this the weight increased steadily from 130 to 240 pounds (59 to 108.8 Kg.). In 1929, at the age of 27, the vision again became impaired, with accompanying epistaxis and frontotemporal headaches. The patient was under observation at Bellevue Hospital for six weeks, where he received high voltage roentgen therapy to the region of the pituitary without improvement. The headaches, epistaxis and visual impairment became gradually worse and he noticed that he did not perspire even during the hottest days of summer. Sexual impotence also developed. In 1931, he had attacks of vertigo and dyspnea while walking. Four or five months prior to his admission to the hospital there was dependent edema of the legs, which disappeared with rest in bed. He also had occasional attacks of severe cramplike pains in the lower extremities.

The patient had never had axillary hair and had very little pubic hair. He began to shave at about the age of 25 and thereafter shaved every three or four

weeks. During the past thirteen years he had slept more than other people. His voice had always been high-pitched. The family history was without significance.

General Examination.—The patient was markedly obese, the obesity being most marked in the mammary region, the abdomen and the hips. The fingers tapered. The axillary hair was absent; pubic hair was sparse and showed the female type of distribution. The penis was small and the testes were atrophic. There were some features typical of hyperpituitarism—thick lips, slight prominence of the jaw and spacing of the teeth. The skin was dry and scaly. There were numerous small vascular nevi over the upper part of the chest. A systolic hemic murmur was heard over the entire precordium. There was pitting edema of the ankles. Ulceration of the left side of the nasal septum was present. The blood pressure was 92 systolic and 56 diastolic.

Neurologic Examination.—The sense of smell was absent bilaterally. There was a high degree of bilateral myopia, with myopic crescents, bilateral optic atrophy, left homonymous hemianopia and diminution in visual acuity which was more marked on the left side. The patient was able to count fingers on the left at about 8 inches (20 cm.) and on the right at about 30 inches (76 cm.). He had difficulty in converging the left eye. The left palpebral fissure was wider than the right, and there was slight weakness of the lower part of the face on the right side. At times a questionable Babinski sign was elicited on the left. Besides general sluggishness and torpor there were no mental changes.

Laboratory Data.—Examination of the blood disclosed a marked secondary anemia. The following values were obtained: red cells, 2,000,000; white cells, 8,000; hemoglobin, 22 per cent; color index, 0.55; polymorphonuclear leukocytes, 70 per cent; eosinophils, 1 per cent; lymphocytes, 26 per cent; monocytes, 3 per cent; anisocytosis, poikilocytosis and microcytosis; platelets, 350,000; plasma, 80 per cent; formed elements, 20 per cent; volume, 55 cc. per kilogram of body weight; coagulation time, three and five-tenths minutes; bleeding time, three minutes; serum calcium, 10.2 mg. per hundred cubic centimeters; cholesterol, 177 mg. and urea nitrogen, 9.9 mg. The sugar tolerance test revealed the following values for blood sugar: after fasting, 95 mg. per hundred cubic centimeters; one hour after ingestion of 100 Gm. of dextrose, 159 mg., and two and one-half hours after ingestion of dextrose, 153 mg. The spinal fluid was under a pressure of 180 mm. of water and was clear and colorless; there was no block, and tests for globulin and sugar were slightly positive. There were 2 cells per cubic millimeter; the total protein content was 34.1 mg. per hundred cubic centimeters; the Wassermann reaction was negative, and the gum mastic curve, 0000000000. The urine was pale and clear; the specific gravity in the concentration test was from 1.007 to 1.009; tests for albumin and sugar gave negative results; microscopically, the appearance was normal. The basal metabolic rate at various periods was —36, —43 and —23 per cent.

Roentgen Examination.—The roentgenogram of the skull revealed marked increase in the visible markings of the vault. The sella was well visualized and shallow. There was no destruction of the floor or of the clinoid processes. The pelvis disclosed moderate hypertrophic arthritis involving both sacro-iliac and both hip joints. The head of the right femur was flattened, and a small, irregular area of bone absorption (cyst) was seen in the region of the head and neck. Surrounding this area was a small amount of bone condensation. There was scoliosis of the lumbar portion of the spine.

Course.—During the stay in the hospital the patient had a consistently low temperature. On only two occasions in the last three months of life did the tempera-

ture rise as high as 99.8 F. (in January 1933). During the greater part of the month of January the rectal temperature remained at about 92.5 F. During this period the maximum output of fluid was 3,500 cc., and the minimum, 950 cc. During the month of February the maximum temperature was 96.6 F., and the minimum, 90.8 F., the average being about 93 F. The maximum intake and output of fluid during this period was 2,240 cc., and the minimum, 650 cc. On several occasions the intake and output of fluid was as much as 3,900 cc. At intervals 0.5 cc. a solution of the posterior lobe of the pituitary was given twice daily hypodermically, resulting in a considerable reduction in the intake and output of fluid and occasionally in a rise in temperature of 1 F. During March the minimum temperature was 90.6 F. and the maximum 95.6 F. On February 16 otitis media developed on the right side with perforation of the right ear drum. Roentgen examination showed destruction of mastoid cells. At this time the patient's temperature rose to 96 F. He refused operation for this condition, and the process subsided under local treatment.

Influence of Hot and Cold Water Baths on the Oral Temperature, Heart Rate and Blood Pressure of a Patient with a Hypothalamic Lesion and Hypothermia

Hour, P.M.	Temperature of Bath, F.	Oral Temperature, F.	Heart Rate	Blood Pressure Readings		Comment
				Systolic	Diastolic	
			Influence of Hot Water Bath			
3:55	96	98.6	66	98	70	
4:00	96	98.2	68	96	70	
4:15	106	97.2	72	90	64	Redness of forearms; restlessness; alert mentally
4:20	108	100.1	100	90	30	Redness extending; patient complained of heat; restlessness; alert mentally
4:30	100	99.9	104	90	30	
4:40	96	99.8	96	90	30	
			Influence of Cold Water Bath			
3:40	80	93.6	64	90	44	
3:45	76	94.0	74	110	64	Shivering; blue finger tips
3:55	76	94.2	74	110	64	Shivering; blue finger tips
4:00	70*	94.2	86	112	64	Shivering; blue finger tips

* The patient could not tolerate this or lower temperatures.

On April 7, 1933, the rectal temperature fell below 90 F. and could not be registered with the ordinary clinical thermometer. On several occasions the patient became disoriented and irrational; these episodes usually disappeared within twenty-four hours. It is worth mentioning that starvation for twenty-four hours did not produce this reaction, nor did it lower the blood sugar below 110 mg. per hundred cubic centimeters. Immersion in a hot water bath of temperatures as high as 108 F., as indicated in the table, caused a rise in the oral temperature to 100.1 F., a rise in the pulse rate and a fall in the systolic and the diastolic blood pressure. At this time there was greater mental alertness. Immersion in a cold water bath produced a rise in the oral temperature from 93.2 F. to 94.2 F. and a rise in the pulse rate and in the blood pressure (table). Subcutaneous administration of atropine sulphate produced little or no effect on the blood pressure. Headaches and epistaxis increased in severity. The patient died on the morning of April 10, 1933.

The report of the necropsy follows.

Macroscopic Examination of the General Organs.—The body was that of a markedly obese, pale white man, 160 cm. long, in a state of semirigor mortis. There were a few fine hairs on the chin and chest. Pubic hair was scanty. The

skin was soft, pale and dry. Several raised nevi were present on the chest. The neck was short and the pelvis wide. A large amount of fat was present over the buttocks and lower portion of the abdomen; the fat of the lower part of the abdomen hung like a large apron. There was a large amount of epicardial fat, which invaded the musculature of the right ventricle. The lungs revealed a bronchopneumonic process. The liver was very firm and the surface finely nodular; the nodules on the inferior surface were slightly larger than elsewhere. The organ cut with increased resistance. The intervening fibrous tissue between the small lobules was firm, grayish white and larger in amount than in the usual hepatic lobule. The pancreas and suprarenals were normal. The testes weighed 23 Gm. and were about one-half the normal size. The seminal vesicles were small and empty. The pituitary gland was normal. The esophagus and stomach contained several tubular clots of blood. The submucosal veins of the esophagus were considerably dilated, but points of rupture could not be seen. There were a few scattered punctate hemorrhages and superficial erosions of the mucosa of the stomach, but no ribbed ulcerations. The head of the right femur was slightly flattened. On sawing through the anterior surface of the head of the femur, several areas of rarefaction were noticed in the cancellous bone. Similar small areas of rarefaction were also observed in the cancellous bone in the lumbar and lower dorsal vertebrae. The sella turcica appeared normal. The posterior clinoid processes were not eroded.

Microscopic Examination of General Organs.—There was no spermatogenesis in the testes; the stroma was increased, but the Leydig cells were few. In the anterior part of the pituitary the chromophobe cells were slightly more numerous than the acidophils; the latter were small and showed only a few degenerative forms. The basophils were few and occurred singly rather than in small groups. The stroma was slightly increased. Several colloid cysts were noted in the pars anterior. There was an unquestionable increase in the density of the glia tissue in the pars posterior. The thyroid, parathyroids and suprarenals were normal. The area of bone absorption in the head of the right femur consisted of fibrillary connective tissue replacing the trabeculae of bone. Two of the trabeculae of bone showed production of cartilage. The marrow was fatty. The lumbar portion of the spine disclosed an area of bone absorption.

Macroscopic Examination of the Brain.—The brain weighed 1,420 Gm. The vessels were slightly engorged. There was a reddish-brown, firm tumor, measuring 2.5 by 1.75 cm., between the floor of the third ventricle and the sella turcica (fig. 2); it extended from the optic nerves to the mamillary bodies. Part of the optic nerves, the chiasm and the optic tracts were embedded in the tumor. The two olfactory tracts were compressed, the left more than the right. All the other cranial nerves were intact. The internal carotid and middle cerebral arteries were flattened and lay over the surface of the tumor. The callosal branches of the anterior cerebral artery were adherent to the tumor (fig. 2). The spinal cord was not removed. The brain was cut sagittally in halves. In sagittal section the neoplasm appeared hemorrhagic with a small necrotic area in the center. Practically the entire floor of the third ventricle was destroyed by the neoplasm (fig. 2). The optic nerves and tracts were partly destroyed and partly embedded in the tumor. The third ventricle in the sagittal view was slightly constricted. The two hemispheres were approximated, and the brain was cut coronally. The tips of the anterior horns of the lateral ventricles were constricted. In a coronal section through the anterior third of the globus pallidus, the third ventricle could barely be visualized; whatever was left was filled by the tumor. In a section through the mamillary bodies,

the third ventricle was constricted; its floor and the left mamillary body were destroyed. The right mamillary body appeared slightly hemorrhagic.

Microscopic Examination of the Brain.—Coronal sections from the anterior third of the neostriatum to the aqueductal region were cut serially and stained by Weil's modification of the myelin sheath stain, cresyl violet and the Davenport modification of Bielschowsky's method. A section of the tumor was stained by the hematoxylin-eosin method.

Section Through the Anterior Third of the Neostriatum: The neoplasm at this level (fig. 3*A*) destroyed the following structures: part of the right tuberculum olfactorium, the optic chiasm, more on the right side than on the left, and the right gyrus subcallosus. The fibers of the right septum pellucidum were partially demyelinated. With a high power lens, a few normal fibers could still be seen on the

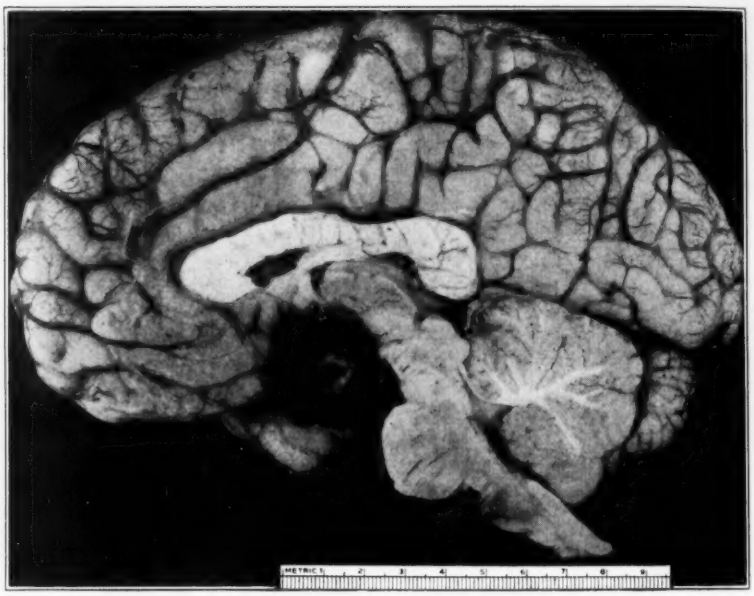

Fig. 2.—Angioma below the floor of the third ventricle, extending from the optic nerves to the mamillary bodies. Part of the optic nerves, optic chiasm and optic tracts and the callosal artery, a branch of the anterior cerebral, are embedded in the angioma.

left side of the optic chiasm. Most of the remaining fibers were demyelinated. Disintegration of myelin sheaths and axis-cylinders, which were replaced by compound granular corpuscles and microglia cells, was also noted. In the preparations stained with cresyl violet, the tumor invaded slightly the gyrus subcallosus, part of the tuberculum olfactorium and the right anterior pole of the optic chiasm. At the point of invasion there were a barrier of proliferated and calcified capillaries and a zone of giant astrocytes (fig. 4). In the zone of the proliferated capillaries, numerous ganglion cells belonging to the aforementioned structures were identified. Some of the nerve cells were completely destroyed, and others showed a variety of pathologic changes. The greater part of the demyelinated chiasm (fig. 3*A*) consisted of fragments of myelin, compound granular corpuscles

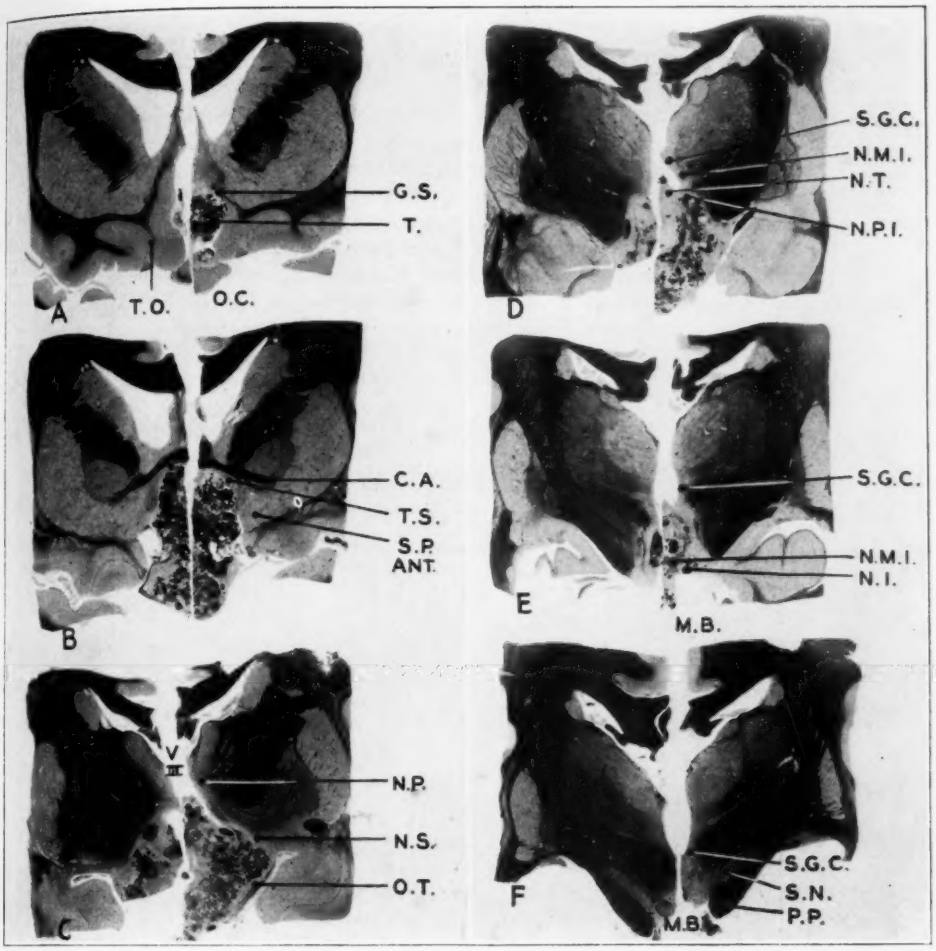

Fig. 3.—*A*, section through the anterior third of the neostriatum. The tumor (*T*) on the right side is destroying part of the right tuberculum olfactorium (*T.O.*), the right optic chiasm (*O.C.*) and the right gyrus subcallosus (*G.S.*). The optic chiasm is extensively demyelinated. *B*, section through the anterior commissure (*C.A.*) and the anterior third of the globus pallidus. The taenia semicircularis (*T.S.*), the substantia perforata anterior (*S.P.Ant.*) and part of the stria olfactoria lateralis are destroyed. The most oral part of the nucleus paraventricularis in this section is also partly invaded by the neoplasm. *C*, section through the anterior third of the thalamus and third ventricle. Part of the ansa lenticularis, the right and left optic tracts, the nuclei supra-optici (*N.S.*) and the nuclei tuberis are invaded by the tumor. The right nucleus paraventricularis (*N.P.*) and part of the right columna fornicis are also slightly involved. The right optic tract (*O.T.*) may be seen embedded in the neoplasm. *D*, section through the infundibulum. The right columna fornicis, tractus supra-opticus, nuclei tuberis (*N.T.*) and nucleus pallido-infundibularis (*N.P.I.*) and nucleus mamillo-infundibularis (*N.M.I.*), part of the nucleus supra-opticus and the greater part of the substantia grisea centralis (*S.G.C.*) are destroyed at this level. *E*, section through the anterior part of the mamillary bodies. The right mamillary body (*M.B.*), nucleus intercalatus (*N.I.*), nucleus mamillo-infundibularis (*N.M.I.*) and substantia grisea centralis (*S.G.C.*) are destroyed. *F*, section through the posterior part of the mamillary bodies (*M.B.*). At this level the right mamillary body, the mesial part of the right substantia nigra (*S.N.*) and the right pes pedunculus (*P.P.*) and substantia grisea centralis (*S.G.C.*) are slightly involved.

and blood pigment. In the Bielschowsky preparations the axis-cylinders in the zone of destruction were fragmented, swollen and corkscrew in appearance.

Section Through the Anterior Commissure and the Anterior Third of the Globus Pallidus (fig. 3*B*): The taenia semicircularis, the optic chiasm, the substantia perforata anterior and part of the right stria olfactoria lateralis were destroyed by the neoplasm. In the cresyl violet preparations the most oral part of the nucleus paraventricularis and of the nucleus supra-opticus could be visualized. The tumor invaded part of the paraventricular nucleus. A barrier of proliferated capillaries and astrocytes between the tumor and the nucleus paraventricularis was noted as in the previous section (fig. 5*B*). The nucleus supra-opticus at this level was spared. The optic chiasm was completely destroyed by the tumor (fig. 3*B*). Evidences of structures belonging to the optic chiasm—glia cells, macroglia and microglia, broken-down myelin sheaths and axis-cylinders—could

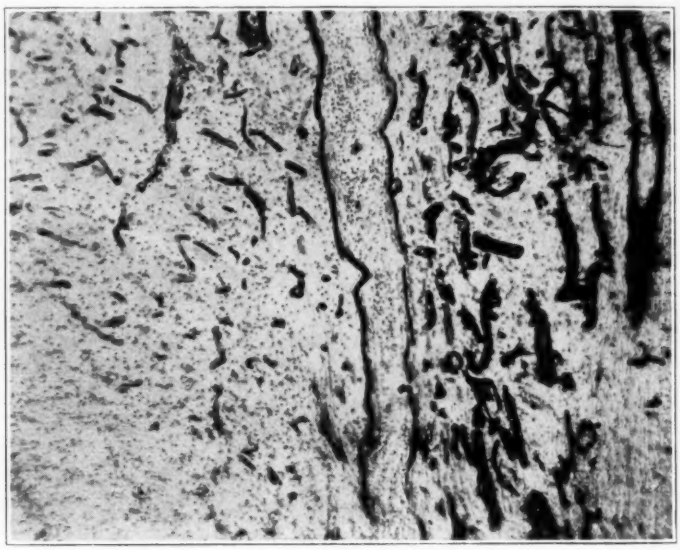

Fig. 4.—Barrier of proliferated and calcified capillaries between the angioma and the neural structures. Cresyl violet stain; × 90.

be identified within the tumor tissue. The temporal lobes adjacent to the tumor showed an increase in the number and hypertrophy of the microglia cells. Some nerve cells in this convolution disclosed chromatolytic changes.

Sections Through the Anterior Third of the Thalamus and the Third Ventricle (fig. 3*C*): The tumor invaded part of the right ansa lenticularis, the optic tracts, the nuclei tuberis and the nuclei supra-optici, more on the right than on the left. The right nucleus paraventricularis and part of the right columna fornicis were also slightly implicated. The right optic tract could be identified and was embedded in the neoplasm (fig. 3*C*); the left was completely destroyed. With high power magnification, the same pathologic changes were noted as in the sections already described. There was a barrier of proliferated capillaries and astrocytes between the neoplasm and the structures involved. The same process was observed in the supra-optic nuclei (fig. 6). Within the area of proliferated capillaries the nerve cells belonging to the supra-optic nuclei could be identified (fig.

6). Some of these were completely destroyed; others showed various pathologic changes, and still others appeared merely as shadow cells (figs. 6 and 7 *B*). The nerve cells of the supra-optic nucleus, situated more laterally, disclosed marked chromatolytic changes; the larger Nissl granules, which are collected normally at the periphery of the cell, were gone (fig. 7 *B*). Well preserved nerve cells of this nucleus were found only near the nucleus basalis. The nerve cells of the nuclei of the tuber were completely destroyed, and few of them could be identified (fig. 8). The paraventricular nerve cells were much better preserved in this section than in the preceding sections, although a few showed pathologic changes (fig. 5 *B*). Some of the nerve cells of the substantia grisea centralis had undergone changes similar to those of the supra-optic nuclei. In Bielschowsky prepara-

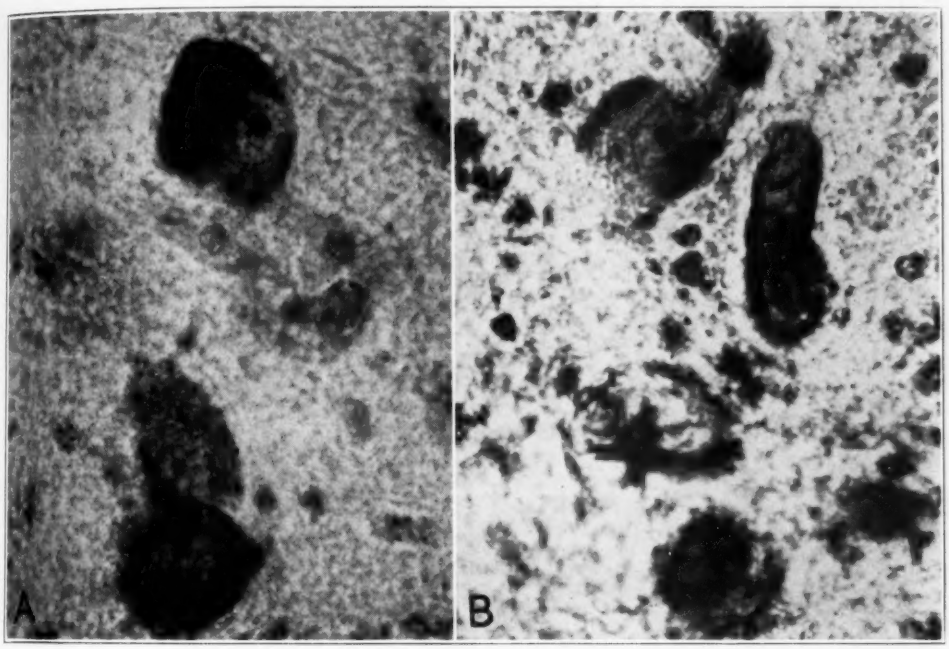

Fig. 5.—*A*, normal nerve cell from the nucleus paraventricularis; *B*, pathologic nerve cell from the nucleus paraventricularis. Cresyl violet stain; × 600.

tions the fibers of the tractus supra-opticus hypophyseus were partially destroyed, though intact axis-cylinders could still be identified.

Section Through the Infundibulum: The neoplasm destroyed the following structures: part of the right columna fornicis, the tractus supra-opticus, the nuclei tuberis, the nuclei pallido-infundibularis, the nuclei mamillo-infundibularis, the medial parts of the supra-optic nuclei and the greater part of the substantia grisea centralis (fig. 3 *D*). In sections stained with cresyl violet practically all of the nerve cells of the nuclei tuberis were destroyed (fig. 8). The few remaining ganglion cells appeared as shadow cells; the Nissl substance, which normally consists of small granules and is evenly distributed throughout the cytoplasm, had disappeared from most of the nerve cells. The nuclei of the tuber were replaced by glia cells (microglia, *gemästete* glia and astrocytes), blood pigment and proliferated capil-

Fig. 6.—Proliferated blood vessels and destruction of the ganglion cells of the nucleus supra-opticus. Many of the nerve cells appear as phantom or shadow cells. Cresyl violet stain; × 150.

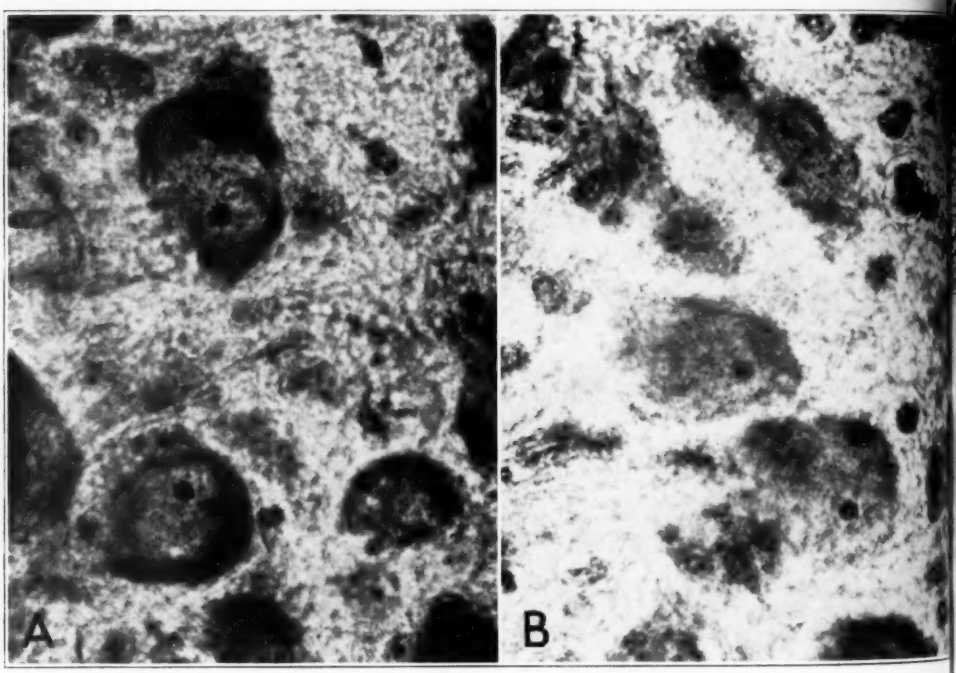

Fig. 7.—*A*, normal nerve cell from the supra-optic nucleus; *B*, pathologic cell from the nucleus supra-opticus. Cresyl violet stain; × 600.

laries (fig. 8). Most of the nerve cells of the mamillo-infundibular and pallido-infundibular nuclei and the intercalate nucleus were also destroyed; the remaining nerve cells either were fragmented or appeared as shadow cells. At this level only a few of the nerve cells of the mesial part of the nucleus supra-opticus were destroyed. Slight chromatolysis, disintegration of cytoplasm, shadow cells and homogeneity were also noted.

The Substantia Grisea Centralis: As is well known, the nerve cells of this structure mingle freely with the nerve cells of the mamillo-infundibular region. Most of the nerve cells of the lower half of this structure, which are normally relatively small with a very small amount of cytoplasm, were destroyed. Those

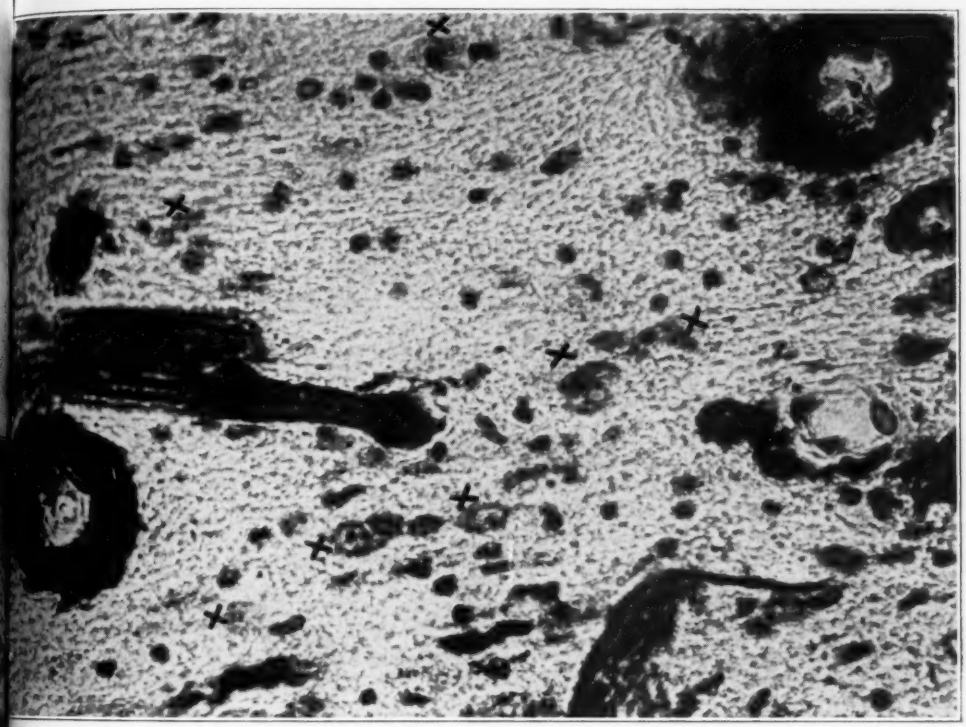

Fig. 8.—Proliferated capillaries in the region of the nuclei of the tuber. Most of the nerve cells have been destroyed; the few remaining appear as shadow cells (*x*).

that could still be identified were fragmented, and others appeared as shadow cells. Part of the infundibulum embedded in the neoplasm could still be seen.

Sections Through the Anterior Part of the Mamillary Bodies: The corpora mamillaria, more on the right side than on the left, the nucleus intercalatus, the nucleus mamillo-infundibularis, the substantia grisea centralis, the right fasciculus mamillothalamicus (fig. 3*E*) and part of the fasciculus thalamicus and decussatio hypothalamicus were destroyed by the neoplasm. In the cresyl violet preparations most of the nerve cells of the right mamillary body were destroyed (fig. 9), while those of the left showed various pathologic changes, such

as shadow cells and complete disintegration. Many nerve cells contained blood pigment (fig. 9). Calcification of nerve cells was also noted. The same destructive process occurred in the nerve cells of the nucleus intercalatus, the nucleus mamillo-infundibularis and the substantia grisea centralis. The wall of proliferated capillaries and astrocytes, as in sections already described, was seen within part of the outer border of the left mamillary body. The caudal part of the nucleus supra-opticus could still be identified in this section, and some of its nerve cells were destroyed. The ganglion cells of the nucleus reuniens and of the nucleus paramedianus were spared.

Section Through the Posterior Part of the Mamillary Body: The same changes were noted as in the preceding sections, except that both mamillary bodies were easily identified at this level and the left mamillary body appeared normal

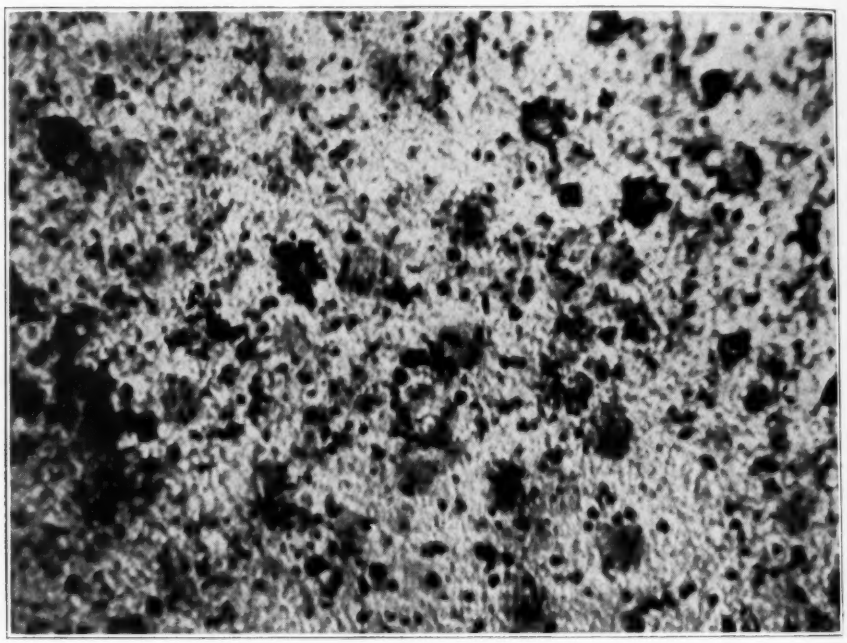

Fig. 9.—Accumulation of pigment in the right mamillary body. Calcified nerve cells are present. Many of the ganglion cells appear as shadow cells.

(fig. 3*F*). The fibers of the fasciculus mamillothalamicus were intact. The mesial part of the right substantia nigra, the right pes pedunculis and the right substantia grisea centralis were partially involved at this level. The right mamillary body showed an increase in the glial cells with pathologic changes in the ganglion cells similar to those in the right mamillary body in the section just described. There was also an increase of blood pigment. A few of the nerve cells of the right substantia nigra had lost their pigment; some were destroyed, and others stained poorly.

Sections of the midbrain, pons, medulla oblongata, cerebellum and spinal cord were normal.

Microscopic Description of the Tumor: The tumor consisted of numerous dilated blood channels, mostly lined by a single layer of endothelial cells. A few

blood vessels had a thin muscular coat. Fully formed vessels were not observed. The intervening tissue between the blood channels consisted essentially of hyalinized connective tissue.

Summary of the Case.—Clinically, the patient had polyuria, polydipsia, adiposogenital dystrophy, hypothermia, hypersomnia, absence of the sense of smell and bilateral primary optic atrophy with diminution in visual acuity. Of these the most outstanding feature was hypothermia. The temperature ranged between 90 and 96.6 F.; at times it was below 90 F. and could not be recorded with the ordinary thermometer. Hot baths produced a marked rise in the body temperature from 93.6 F. to 100.1 F. (table 1); cold baths produced a rise of body temperature of 0.6 F.

Pathologically, an angioma, situated above the sella turcica, compressed the two olfactory bulbs and destroyed the right tuberculum olfactorium, the right gyrus subcallosus, part of the optic nerves, the optic chiasm and tracts and most of the hypothalamic nuclei. The hypophysis was spared. In summarizing the observations on the involved hypothalamic nuclei it is best to treat the nuclei in two divisions: (1) the vegetative nuclei in the region of the tuber cinereum (figs. 1*A* and 3*A*, *B* and *C*) and (2) the vegetative nuclei in the region of the mamillary body (figs. 1*B* and 3*D*, *E* and *F*). As seen in histopathologic sections, the nuclei of the first group that were involved were the supra-optic and paraventricular nuclei, the nuclei tuberis proper, the mamillo-infundibular and pallido-infundibular nuclei and the substantia grisea centralis (figs. 3*A*, *B* and *C*, 5*B*, 7*B* and 8). Of these, only the oral ends of the supra-optic and the paraventricular nuclei were slightly affected. All the other nuclei, especially the nuclei of the tuber, were completely destroyed. The vegetative nuclei in the region of the mamillary body that were partly destroyed were the mamillo-infundibular and intercalate nuclei, the nuclei of the mamillary body (nucleus magnocellularis, nucleus parvocellularis and nucleus mamillaris cinereus) and part of the substantia grisea centralis (figs. 3*D*, *E*, and *F*). The right mamillary body was more involved than the left (fig. 9). A few nerve cells of the right substantia nigra were also implicated. The corpus subthalamicum (corpus Luysii), considered by some as a hypothalamic nucleus, was completely spared.

Correlation of the clinical findings with the pathologic process in the vegetative nuclei should not be difficult. The slight polyuria, polydipsia, adiposogenital dystrophy and hypersomnia were undoubtedly caused by destruction or compression of the vegetative nuclei of the region of the tuber cinereum (paraventricular and supra-optic nuclei) and the tractus supra-opticus hypophyseus. Hypothermia was most likely due to destruction of the nuclei tuberis proper. Disturbances of smell were induced by compression of the olfactory bulbs and partial destruction

of the right tuberculum olfactorium. The optic atrophy and diminution in visual acuity are attributable to destruction and compression of the optic nerves, chiasm and tracts. The slight central facial weakness and the questionable Babinski sign on the left were caused by pressure on the cerebral peduncles.

COMMENT

The case presented is of interest from the point of view of localization of hypothalamic function. It is well established that disturbances in carbohydrate, protein, fat and water metabolism may be caused by lesions of the vegetative centers of the tuber cinereum. That carbohydrate, protein and fat metabolism, elimination of water and the activity of the sweat glands influence heat production is also well known. It is common knowledge that many tumors and other pathologic processes in the region of the floor of the third ventricle are frequently accompanied by hyperpyrexia. It has also been observed that operations in this region are followed at times by a rise in temperature. Complete and sudden emptying of the ventricles, particularly in children, is also associated frequently with hyperthermia. On the other hand, the craniopharyngiomas and the chromophobe adenomas in some patients may cause subnormal temperature, often averaging as low as 97 F.

Experimental evidence for the abnormal production of heat, "hyperpyrexia," has been described by Ott,[3] Barbour,[4] Isenschmid and Krehl,[5] Jakobj and Roemer,[6] Citron and Leschke,[7] Walbaum,[8] Isenschmid and Schnitzler,[9] Keller and Hare [10] and others. Most of these authors have shown that punctures or other types of destruction of the tuber cinereum are usually followed by an elevation of temperature.

3. Ott, I.: Function of Tuber Cinereum, J. Nerv. & Ment. Dis. **18**:431, 1891.

4. Barbour, H. G.: Die Wirkung unmittelbarer Erwärmung und Abkühlung der Wärmezentren auf die Körpertemperatur, Arch. f. exper. Path. u. Pharmakol. **70**:1, 1912.

5. Isenschmid, R., and Krehl, L.: Ueber den Einfluss des Gehirns auf die "Wärmeregulation," Arch. f. exper. Path. u. Pharmakol. **70**:109, 1912.

6. Jakobj, C., and Roemer, C.: Beiträge zur Erklärung der Wärmestichhyperthermie, Arch. f. exper. Path. u. Pharmakol. **70**:149, 1912.

7. Citron, J. B., and Leschke, E.: Ueber den Einfluss der Ausschaltung des Zwischenhirns und das infektiöse und nichtinfektiöse Fieber, Ztschr. f. exper. Path. u. Therap. **14**:379, 1913.

8. Walbaum, H.: Hirnbefunde durch Hirnreizung hyperthermisch gemachter Kaninchen und ihre Beziehungen zur Hyperthermie, Arch. f. exper. Path. u. Pharmakol. **75**:423, 1914.

9. Isenschmid, R., and Schnitzler, W.: Beitrag zur Lokalisation des Wärmeregulation vorstehenden Zentralapparates im Zwischenhirn, Arch. f. exper. Path. u. Pharmakol. **76**:202, 1914.

10. Keller, A. D., and Hare, W. K.: The Hypothalamus and Heat Regulation, Proc. Soc. Exper. Biol. & Med. **20**:1069, 1932.

There is also sufficient experimental evidence to show that the contrary may occur, i. e., a lowering of the body temperature. Christiani,[11] as early as 1885, noticed that the temperature remained unchanged when the corpus striatum was extirpated, but on removal of the optic thalamus the temperature dropped from 3 to 5 degrees C. in the first fifteen minutes after operation. Sawadowsky [12] induced lowering of the body temperature by transection of the brain stem in the region of the corpus striatum, optic thalamus and pons Varolii. When an incomplete section was performed, the temperature rose. Lewisky [13] observed decrease in temperature after transection of the brain stem between the pons and the medulla oblongata. Definite conclusions cannot be drawn from these experiments as the animals died shortly after the operation. The element of shock should be considered as a factor in the lowering of the body temperature in these animals.

Isenschmid and Krehl [5] found that rabbits deprived of the forebrain and the diencephalon commonly lose control of the heat-regulating mechanism; the body temperature of the animal rises or falls with changes in the surrounding room temperature. These authors localized the center for heat regulation in the middle and caudal part of the diencephalon. Leschke,[14] by puncturing the medial part of the subthalamic region in rabbits, produced a disturbance in the heat-regulating mechanism. Following this procedure the rabbits behaved like poikilothermic animals—the body temperature varied with changes in the surrounding temperature. He agreed with the views expressed by Edinger [15] and Karplus and Kreidl [16] that this organ is the center of the sympathetic system. Solari [17] removed the hypophysis in thirty-four dogs and cauterized the region of the tuber in seven others in which the pituitary had previously been removed. The animals without the hypophysis and with lesions of the tuber on the day after the operation had a hyperthermia, the temperature being 40.8 C. (105.4 F.); in from six to eight days the temperature returned to normal levels. Two of the dogs with lesions of

11. Christiani, A.: Zur Physiologie des Gehirns, Berlin, O. Enslin, 1885.

12. Sawadowsky, J.: Zur Frage über die Lokalisation der Wärmeregulierenden Centren im Gehirn und über die Wirkung des Antipyrins auf den Tierkörper, Centralbl. f. d. med. Wissensch. **26**:148, 161 and 178, 1888.

13. Lewisky, P.: Ueber den Einfluss des schwefelsauern Chinins auf die Temperatur und Blutcirculation, Virchows Arch. f. path. Anat. **47**:352, 1869.

14. Leschke, E.: Ueber den Einfluss des Zwischenhirns auf die Wärmeregulation, Ztschr. f. exper. Path. u. Therap. **14**:167, 1913.

15. Edinger, L.: Vorlesungen über den Bau der nervösen Centralorgane des Menschen und der Thiere, Leipzig, F. C. W. Vogel, 1911.

16. Karplus, J. P., and Kreidl, A.: Gehirn und Sympathicus; Zwischenhirns- und Halssympathicus, Arch. f. d. ges. Physiol. **129**:138, 1909; Gehirn und Sympathicus: VII. ibid. **215**:667, 1927.

17. Solari, L. A.: Temperature et réactions thermiques chez les chiens hypophysaires ou à tuber lésé, Compt. rend Soc. de biol. **108**:126, 1931.

the tuber showed marked lowering of temperature (32.5 C. [90.5 F.] in the case of one of them). Of the thirty-four dogs in which the pituitary alone had been removed, only three had a mild degree of hypothermia (temperature, 37.5 C. [99.5 F.]). The author expressed the opinion that the tuber cinereum was perhaps damaged in these three dogs. He concluded that the tuber alone, and not the hypophysis, was concerned with the function of regulation of temperature. Bazett, Alpers and Erb [18] have demonstrated, in experiments on cats, that control of temperature appeared to be associated with the preservation of the hypothalamus just cephalic to the mamillary bodies, the area including the nuclei surrounding the walls of the third ventricle and the infundibular nuclei.

As already stated, except for the fragmentary report of one case by Ratner [19] there are no recorded clinical cases in the literature with such marked persistent lowering of temperature as was present in our case. Ratner's patient had epilepsy for eighteen years and, finally, cachexia hypophyseopriva with an axillary temperature of 35.8 C. (96.4 F.). Ratner did not state how long this low temperature persisted. At autopsy a large meningioma impinging on the inferior temporal lobe and hippocampus and reaching as far as the walls of the third ventricle was found. Ratner concluded that the syndrome was due to interference with the vegetative trophic centers of the midbrain. Obregia, Dimolescu and Constantinescu [20] reported a case in which a craniopharyngioma compressing the floor of the third ventricle caused a lowering of the body temperature to from 35.2 to 36.4 C. (95.4 to 97.5 F.) for a period of ten days. Low temperatures in cases of craniopharyngioma and of chromophobe adenoma recorded by Cushing [21] and others were never much below 97 F.

The determination of the exact nuclear groups in the hypothalamic region responsible for the interference with the temperature-regulating mechanism is a more difficult problem. In our patient, the nuclei which were most severely injured (almost completely destroyed) were the nuclei tuberis and the nucleus mamillo-infundibularis. The nucleus supra-opticus and nucleus paraventricularis were damaged only at the oral ends. The nuclei of the mamillary bodies, especially of the right, although not destroyed completely, were more severely affected than were the supra-optic and paraventricular nuclei. Of interest is the

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18. Bazett, H. C.; Alpers, B. J., and Erb, W. H.: Hypothalamus and Temperature Control, Arch. Neurol. & Psychiat. **30**:728 (Oct.) 1933.

19. Ratner, J.: Tumor des Mittelhirns unter dem Bilde einer pluriglandulären Insuffizienz, Klin. Wchnschr. **4**:599, 1925.

20. Obregia, A.; Dimolescu, A., and Constantinescu, S.: Syndrome infundibulotubérien avec troubles mentaux complexes par tumeur supra-sellaire du troisième ventricule; Étude anatomo-clinique, Encéphale **27**:93, 1932.

21. Cushing, H.: Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

involvement of the mamillary bodies, especially as it has been suggested by some observers that these nuclear masses are responsible for the mechanism of heat regulation. Greving [1] expressed the belief that the nuclei of the tuber regulate temperature. Malone [2] and later Spiegel and Zweig [22] have shown that the nuclei tuberis are phylogenetically more recent in origin than the other nuclear masses of the hypothalamic region. The appearance of the nuclei of the tuber and of heat regulation in mammals at about the same time suggests that the nuclei of the tuber cinereum have something to do with the regulation of body temperature. The complete destruction of the nuclei of the tuber in our case and the loss of control of body temperature favor the views of these authors.

An attempt to correlate the other symptoms attributable to lesions of the hypothalamus may also be of interest. It is by no means settled which nuclei are responsible for the control of water metabolism. Camus and Roussy [23] and Roussy and Mosinger [24] thought that the paraventricular nuclei regulate water metabolism. According to Greving,[1] the supra-optic nuclei alone and possibly also the paraventricular nuclei control this function. Greving [1] stated that the supra-optic nuclei send most of their fibers to the hypophysis, and he expressed the belief that hypothalamic lesions act by mediation of the hypophysis. Bourquin [25] held that the mamillary bodies control water metabolism.

The opinions in regard to sugar metabolism also vary. Le Grand [26] concluded from his experiments that the paraventricular nuclei are concerned with this function. Brugsch, Dresel and Levy,[27] who experimented on cats, stated that the mamillo-infundibular nuclei were affected. Goormaghtigh and de Wulf [28] and de Wulf [29] found that

22. Spiegel and Zweig: Zur Cytoarchitektonik des Tuber cinereum, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **22**:278, 1919.

23. Camus, J., and Roussy, G.: Experimental Researches on the Pituitary Body, Endocrinology **4**:507, 1920; Les syndromes hypophysaires, Rev. neurol. **29**:644, 1922.

24. Roussy, G., and Mosinger, M.: Le tuber cinereum et son rôle dans les principales fonctions du metabolisme; metabolisme de l'eau, des glucides et des lipides, Ann. de méd. **33**:193, 1933.

25. Bourquin, H.: Studies in Diabetes Insipidus, Am. J. Physiol. **79**:362; **83**: 175, 1927; **88**:519, 1929.

26. Le Grand, A.: Les glycosuries nerveuses expérimentales: La glycosurie tubérienne, Thèse de Paris, 1925.

27. Brugsch, T.; Dresel, K., and Levy, F. H.: Die zentrale Regulation des Zuckerstoffwechsels, Verhandl. d. deutsch. Kong. f. inn. Med. **33**:258, 1921.

28. Goormaghtigh, N., and de Wulf, A.: Dégénérescence mucocytaire du cerveau moyen et intermédiaire suivie de glycosurie, Compt. rend. Soc. de biol. **100**:442, 1929.

29. de Wulf, A.: La signification des lesions tubériennes dans les troubles du métabolisme des hydrates de carbone, Arch. internat. de pharmacodyn. et de thérap. **40**:147, 1931.

injury to the paraventricular nuclei did not induce diabetes. Beattie, Brow and Long [30] thought that the excitosecretory center of the medulla of the suprarenal gland, which is also a glycoregulator, is represented in the posterior part of the paraventricular nuclei. Lhermitte [31] described cases of arterial softening of the paraventricular nuclei and nuclei tuberis with diabetic glycosuria.

Disturbances in lipoid metabolism, adiposity and genital dystrophy induced by lesions of the tuber cinereum were produced by Camus and Roussy,[23] Houssay,[32] Bailey and Bremer,[33] Smith [34] and others. In contrast to some of the experiments on sugar or water metabolism, no one has so far succeeded in demonstrating specific nuclear involvement. It should be mentioned that Erdheim,[35] as early as 1909, considered the diencephalon as the regulating center for fat metabolism. Cushing's experimental work [36] on the production of adiposity by ablation of the posterior lobe is well known; whether the tuber or the pathways connecting the pituitary and the region of the tuber were damaged in the experiments was not determined at that time. The exact localization of specific nuclear control in the metabolism of mineral salts and in the mechanism of sleep is even more difficult to determine.

It is well known that the tuber cinereum acts in unison with other endocrine glands, such as the hypophysis, the thyroid and the suprarenals. The tractus supra-opticus, which connects the supra-optic nuclei with the hypophysis, is the only well established neural connection of the tuber with the endocrine system. The induction of the syndromes of the tuber by hypophyseal lesions and by the action of extracts of the posterior and of the anterior lobe suggests the possibility of neurohormonal action. We are, therefore, safe in stating that the hypothalamic region

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30. Beattie, J.; Brow, G. R., and Long, C. N. H.: Physiological and Anatomical Evidence of the Existence of Nerve Tracts Connecting the Hypothalamus with Spinal Sympathetic Centers, Proc. Roy. Soc., London, s.B **106**:253, 1930.

31. Lhermitte, J.: Le diabète insipide d'origine infundibulaire: étude anatomico-clinique, Compt. rend. Soc. de biol. **86**:579, 1922; La polyurie infundibulaire: le diabète insipide syphilitique, Ann. de méd. **11**:89 (Feb.) 1922; Les syndromes infundibulo-tubériens syphilitiques, Encéphale **27**:628, 1932.

32. Houssay, B. A.: Pituitary Body and Polyuria, Endocrinology **2**:94, 1918.

33. Bailey, P., and Bremer, F.: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

34. Smith, P. E.: Hypophysectomy and Replacement Therapy in the Rat, Am. J. Anat. **45**:205, 1930. Smith, P. E., and White, W. E.: Effect of Hypophysectomy on Ovulation and Corpus Luteum Formation in Rabbit, J. A. M. A. **97**:1861 (Dec. 19) 1931.

35. Erdheim, J.: Ueber einen Hypophysentumor von ungewöhnlichem Sitz, Beitr. z. path. Anat. u. z. allg. Path. **46**:233, 1909.

36. Cushing, H.: The Pituitary Body, Philadelphia, J. B. Lippincott Company, 1912.

consists of numerous vegetative nuclear centers which are in intimate connection with the endocrine glands and are also concerned with the regulation of metabolism.

SUMMARY AND CONCLUSIONS

A case is described in which clinically the patient presented slight polyuria and polydipsia, adiposogenital dystrophy, hypersomnia and a prolonged subnormal temperature. For at least three months the temperature ranged from below 90 to 96.6 F., the average temperature being about 92.5 F.

Pathologically, an angioma, situated in the floor of the third ventricle, destroyed partially the oral ends of the supra-optic and paraventricular nuclei and the right mamillary body. The nuclei tuberis proper were destroyed throughout their entire extent. In addition, the following hypothalamic nuclei were implicated in the destructive process: the mamillo-infundibular and pallido-infundibular nuclei, the substantia grisea centralis and the intercalate and interfornicate nuclei.

An attempt was made to attribute the syndrome presented by this patient to the involvement of the hypothalamic nuclei. The slight polyuria and polydipsia were most likely produced by the partial destruction of the paraventricular and supra-optic nuclei. The extreme subnormal temperature is ascribed to the extensive implication of the nuclei tuberis proper and of the mamillary bodies.

CARBOHYDRATE METABOLISM

THE EFFECT OF HYPOTHALAMIC LESIONS AND STIMULATION OF THE AUTONOMIC NERVOUS SYSTEM

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The frequent association of acromegaly and diabetes mellitus first drew attention to the possible relationship of the pituitary body to carbohydrate metabolism. The experimental and clinical investigations of Goetsch, Cushing and Jacobson,[1] which showed that states of hypopituitarism are accompanied by an increased tolerance for sugars, appeared to be a strong argument in favor of the view that this clinical condition is the opposite of acromegaly. In a later investigation of this matter Weed, Cushing and Jacobson[2] concluded that the glycosuria produced in animals by stimulation of the superior cervical sympathetic ganglion was effected by liberation of a pituitary hormone released by impulses which reached the hypophysis. More recently added impetus has been given to the study of this relation between the hypophysis and carbohydrate metabolism by the work of Houssay and Biasotti.[3]

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1. Goetsch, E.; Cushing, H., and Jacobson, C.: Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri, Bull. Johns Hopkins Hosp. **22**:165, 1911.

2. Weed, L. H.; Cushing, H., and Jacobson, C.: Further Studies on the Rôle of the Hypophysis in the Metabolism of Carbohydrates: The Anatomic Control of the Pituitary Gland, Bull. Johns Hopkins Hosp. **24**:40, 1913.

3. Houssay, B. A., and Biasotti, A.: (*a*) The Hypophysis, Carbohydrate Metabolism and Diabetes, Endocrinology **15**:511, 1931; (*b*) La diabetes pancreática de los perros hypofisoprivos, Rev. Soc. argent de biol. **6**:251, 1930; (*c*) Sobre la substancia hypofisaria que refuerza la diabetes pancreática, ibid. **7**:3, 1931; (*d*) Hypophysectomie et diabète pancréatique chez le crapaud, Compt. rend. Soc. de biol **104**:407, 1930; (*e*) Pankreasdiabetes und Hypophyse beim Hund, Arch. f. d. ges. Physiol. **227**:664, 1931; (*f*) Les troubles diabétiques chez les chiens privés d'hypophyse et de pancréas, Compt. rend. Soc. de biol. **105**:121 and 124, 1930. (*g*) Houssay, B. A.; Biasotti, A., and Rietti, C. T.: Action de la substance diabétogène de l'extrait anté-hypophysaire dans diverses conditions physiologiques, ibid. **115**:323, 1934.

These investigators have shown that in hypophysectomized dogs and other species removal of the pancreas is not followed by glycosuria and hyperglycemia such as occur in normal animals. They have shown also that after removal of the pancreas in hypophysectomized toads and dogs, implantation of the anterior lobe of the pituitary gland establishes a diabetes such as occurs after pancreatectomy in normal animals.

Recently, Cushing [4] has drawn attention to Bramwell's statement, made as early as 1888, that the hypothalamus might well participate in the symptomatology of lesions of the pituitary gland. The experiments of Camus and Roussy [5] and of Bailey and Bremer,[6] which disclosed that polyuria could be produced by injuries restricted to the tuber cinereum, revived the criticism, first raised by Aschner,[7] of experimental hypophysectomies. In spite of attempts to improve the technic of this operation, it would appear that in dogs the criticism is still valid. In lower forms, such as the rat, it may be accepted that accurately placed experimental lesions may be made which result in strictly hypothalamic or pituitary symptoms.

The controversy over the rôle played by the hypothalamic region and the hypophysis itself in these and similar experiments has been a long one with sharply divided opinions on each side. It is conceivable that both structures may play a definite rôle.

Our experimental work may be divided into two parts. First we became interested in knowing whether or not an accurately placed lesion in the hypothalamus made with the Horsley-Clarke stereotaxic instrument would control the development of hyperglycemia and glycosuria following removal of the pancreas. Second, we wished to repeat the work of Weed, Cushing and Jacobson to determine whether or not, as Cushing has suggested, the glycogenolytic responses obtained by stimulation of the superior cervical sympathetic ganglion might not originate in the hypothalamic region.

EFFECT OF HYPOTHALAMIC LESIONS

Houssay and Biasotti have shown that removal of the pancreas in toads is followed by intense diabetes. However, if the entire hypophysis or its anterior lobe is removed or the infundibulum is injured,

4. Cushing, H.: Pituitary Body and Hypothalamus, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

5. Camus, J., and Roussy, G.: Pituitary Syndromes, Rev. neurol. **38**:622, 1922.

6. Bailey, P., and Bremer, F.: Experimental Diabetes Insipidus, Arch. Int. Med. **28**:773 (Dec.) 1921.

7. Aschner, B.: On the Function of the Pituitary, Arch. f. d. ges. Physiol. **146**:1, 1912.

diabetes is delayed or prevented entirely. When the anterior lobe of the pituitary gland was implanted beneath the skin following such operations, diabetes appeared as in a normal animal. These experiments were repeated on dogs, and it was shown that hypophysectomy previous to, or following, pancreatectomy diminished the diabetic state. On the contrary, lesions of the tuber cinereum induced with galvanocautery which extended from behind the hypophysis to the mamillary bodies did not hinder the development of pancreatic diabetes.

Barnes and Regan [8] repeated these experiments on two animals and obtained similar results. They were able to produce hyperglycemia and glycosuria in their animals by the injection of anterior lobe extracts.

In our first series of animals, a complete pancreatectomy was performed on twelve cats. The removal of all of the pancreas has been verified in this and subsequent series by gross dissection and by microscopic examination of the related viscera for accessory glandular tissue. Eleven of the pancreatectomized animals died within one week, either of a severe diabetic state in spite of the use of insulin, or as the result of an acute infection of the upper respiratory tract. One animal was given 4 units of insulin immediately following the operation and four doses of 3 units each on the following day. On the second postoperative day, a lesion was made in this animal by the Horsley-Clarke apparatus with the purpose of damaging the hypophysis. Following this procedure 8 units of insulin was given on the first day, 7 units on the second day, 4 units on the third day and none thereafter. This animal lived for fifty-nine days and was then killed. Protocols of these experiments are as follows:

Cat 10.—A pancreatectomy was done on May 3, 1933; one dose of 4 units of insulin was given on May 3 and four doses of 3 units each on May 4; a lesion was made with the Horsley-Clarke apparatus on May 5; doses of 8, 7, and 4 units of insulin were given on May 6, 7 and 8, and the animal was killed on July 2.

The blood sugar rose from a preoperative level of 74 to 200 mg. when the lesion in the brain was made. Following this procedure it was 250 mg., but it then dropped steadily to 100 mg. on the fifth postoperative day. It remained between 70 and 120 mg. except on two occasions, when it fell to 40 mg. on the seventh postoperative day and 30 mg. on the twelfth. Because of a fear of hypoglycemia, 10 Gm. of a sugar solution was given by stomach tube (fig. 1).

Immediately following the lesion of the brain the cat's vision was disturbed, as was evidenced by the fact that the animal did not blink or draw away the head when striking movements were made toward the face. The right pupil was larger than the left, but both reacted slightly to light. Little emotion was displayed during the first two weeks when loud noises were made, a stomach tube was inserted or blood was withdrawn from the veins. The reactions to these stimuli appeared to be more nearly normal by the end of the third week.

8. Barnes, B. O., and Regan, J. F.: The Relation of the Anterior Pituitary to Carbohydrate Metabolism, Endocrinology **17**:522, 1933.

Pathologic Anatomy.—The needle had entered in the midline, passing through the third ventricle. The lesion destroyed a segment of the middle of the anterior lobe of the hypophysis and a small part of the pars nervosa, with slight damage to the pars tuberalis. The infundibulum seemed to be at least partially blocked by scar tissue and the pars tuberalis appeared slightly hypertrophied, with acini greatly distended by colloid. The space separating the pars intermedia from the anterior lobe was also markedly distended and contained a large amount of homogeneous material. There was also some damage to the ventral part of the tuber cinereum, extending from the optic chiasm to the opening of the infundibulum. This lesion was situated symmetrically in relation to the midline. Nerve structures which were damaged or destroyed included the postoptic commissures, the ventral periventricular nuclei and the gray substance of the tip of the tuber cinereum just rostral to the infundibulum. The last-mentioned structure was penetrated by the needle and contained a small amount of blood. Theoretically, the tractus hypothalamicohypophyseus should have been damaged severely. The nucleus filiformis was normally developed, but the nucleus tangentialis (supraopticus) showed some apparent loss of cells in its rostral portion and was poorly

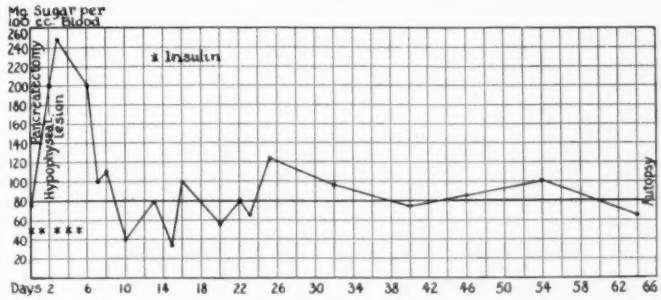


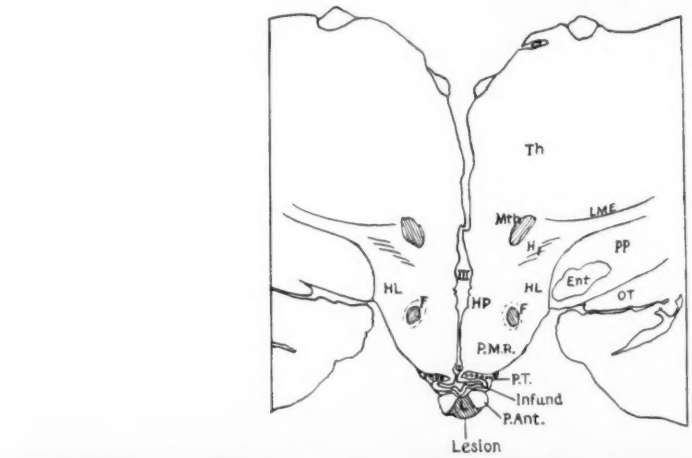
Fig. 1 (cat 10).—Blood sugar determination in a pancreatectomized cat which received injections of insulin, followed by a hypothalamic lesion. The determinations were made on an average of every forty-eight hours. In this and the accompanying figures only the determinations which show a definite rise and fall are included, and the amounts throughout are expressed in milligrams per hundred cubic centimeters. Specimens of blood were obtained at approximately the same time of day and the character and amount of food were controlled.

developed in its caudal portion. The remaining hypothalamic nuclei were intact (fig. 2). No pancreatic tissue was observed on gross dissection or microscopic examination.

Comment.—The deliberate attempt to injure the hypophysis in this animal was followed by results in complete agreement with those of Houssay and Biasotti. With the pancreas removed and after the lesion had been made, this animal did not show a blood sugar level above 120 mg. for fifty-four days, in spite of an entire absence of insulin. However, the lesion was not one of the hypophysis alone, since the ventral part of the tuber cinereum, the postoptic commissures and the ventral periventricular nuclei were involved. We have been unable to find photomicrographs of the lesions of the brains of the animals reported

by Houssay and Biasotti or by Barnes and Regan. It is possible that in their animals similar lesions adjacent to the hypophysis were also present.

In the light of the work of those [9] who believe that the products of secretion from the pituitary body pass from the pars intermedia by way



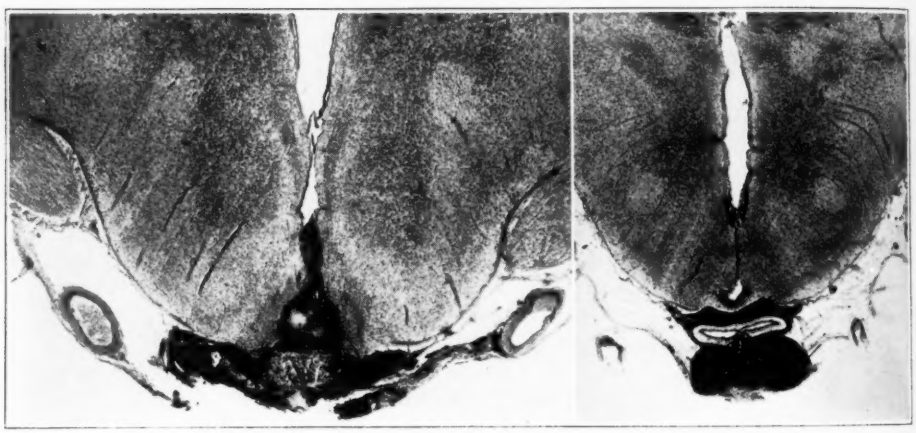


Fig. 2 (cat 10).—Medial lesion of the hypothalamus. *Th* represents the dorsal thalamus; *III*, the third ventricle; *LME*, the external medullary lamina; *PP*, the pes pedunculi; *Ent*, the nucleus entopeduncularis; *OT*, the optic tracts; *HL*, the lateral hypothalamic area; *MTH*, the mamillothalamic tract; *HP*, the posterior hypothalamic area; *P.T.*, the pars tuberalis; *Infund*, the infundibulum, and *P.Ant.*, the pars anterior of the hypophysis.

9. Herring (The Histological Appearances of the Mammalian Pituitary Body, Quart. J. Exper. Physiol. **1**:121 and 181, 1908) has described "hyaline bodies" which he looked on as the secretory product of the pars intermedia and which make their way through the nerve tissue into the infundibular cavity of cats. Cushing and Goetsch (Concerning the Secretion of the Infundibular Lobe of the Pituitary Body and Its Presence in the Cerebrospinal Fluid, Am. J. Physiol. **27**: 60, 1910) made similar observations on dogs.

of the tissue spaces in the pars nervosa to stimulate the tuberal and other anterior hypothalamic nuclei, it is interesting to note that in this animal the infundibulum was partially blocked and that the space separating the pars intermedia from the anterior lobe was distended and contained a large amount of homogeneous material. It has been suggested that as the result of nerve impulses from hypothalamic nuclei ripened secretory cells are cast off which invade the pars nervosa and become hyaline bodies. The latter then make their way through the pars nervosa toward the infundibular cavity.

In a second series of animals, eleven cats were studied. Lesions had been made in the hypothalamus by means of the Horsley-Clarke stereotaxic apparatus at periods varying from one to two months

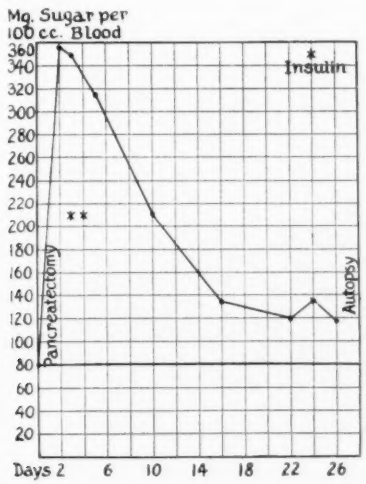


Fig. 3 (cat 63).—Blood sugar determinations in a pancreatectomized cat which thirty days previously had received a lesion of the hypothalamus. Injections of insulin were given on the third and fourth days following pancreatectomy.

previous to removal of the pancreas. Of these animals, seven died after an average postoperative period of three days following pancreatectomy. One animal lived seventy-four days and was then killed; another died of enteritis thirty days after the pancreas had been removed; a third cat was killed on the fourteenth day, and the fourth on the twenty-second day.

CAT 63.—A hypothalamic lesion was made on April 20, 1933; pancreatectomy was performed on May 19, and 3 units of insulin was given on May 22 and 23. The animal was killed on June 17.

The blood sugar rose from 77 to 246 mg. in the five days immediately following the hypothalamic lesion. It then returned to normal where it remained until the pancreatectomy, thirty days later. Following removal of the pancreas the blood sugar rose to 357 mg. within three days and glycosuria, but no polyuria, was

present. Three units of insulin was given on the third and fourth days, following which there was a gradual drop in the blood sugar. It remained between 118 and 138 mg. from the eighteenth to the twenty-eighth day. There was no glycosuria after the fifth day following removal of the pancreas (fig. 3).

Pathologic Anatomy.—The lesions were symmetrical and situated just caudolateral to the nucleus hypothalamicus ventromedialis, destroying the fornix and

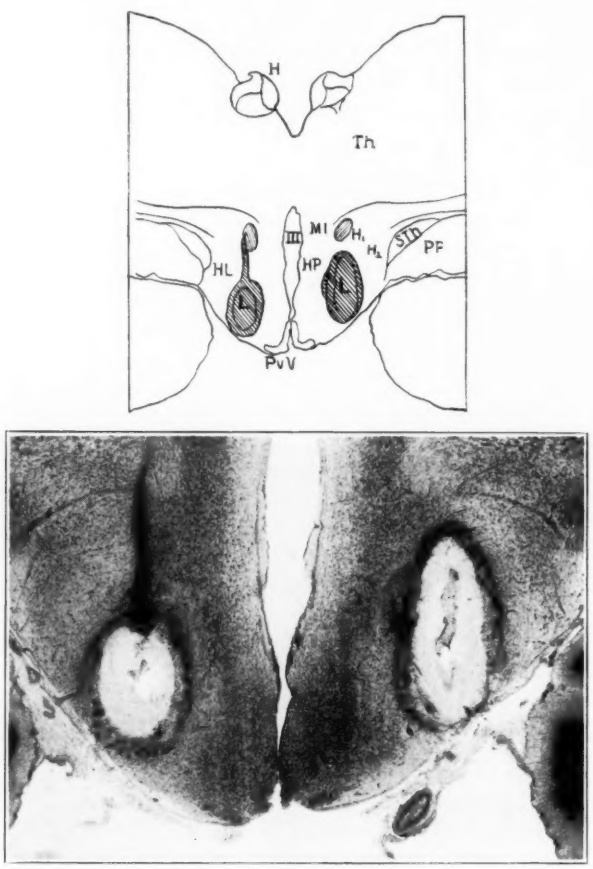


Fig. 4 (cat 63).—Bilateral lesions of the hypothalamus. *PvV* represents the nucleus periventricularis ventralis; H_1 and H_2, the fields of Forel, and *STh*, the nucleus subthalamicus.

perifornical nuclei and slightly affecting the medial borders of the lateral hypothalamic nuclei. They did not approach the third ventricle, but extended ventrally as far as the ventral surface of the tuber cinereum. The opening of the infundibular stalk and its neighborhood were not affected. The tuberomamillary nuclei were but slightly damaged and the lateral mamillary nucleus on the left side was encroached on by the caudal margin of the left lesion. The tangential and filiform nuclei were apparently normal. The hypophysis was unharmed (fig. 4).

The tiny fragments of tissue seen in the abdomen which might be suspected of being accessory pancreatic tissue contained fibrous and lymphoid tissue with some minute, encapsulated bits of peculiar tissue which seemed to contain ducts. These perhaps resembled caricatures of pancreatic tissue, but the resemblance to islets was not striking.

CAT 65.—A hypothalamic lesion was made on April 24, 1933, and pancreatectomy performed on May 19; 1 cc. of an anterior lobe extract was given on July 6 and 7, and daily doses of theelin (100 rat units) from July 12 to July 21. The cat was killed on July 21.

The blood sugar rose from 93 to 113 mg. on the first day following the hypothalamic lesion. Thereafter, until removal of the pancreas on the twenty-sixth day, the blood sugar remained between 80 and 100 mg. It rose to 334 mg. within one week after removal of the pancreas, and a moderate glycosuria was present. The blood sugar then dropped gradually to 88 mg. It remained between 70 and 75 mg. from the fifteenth to the forty-fourth day. On the forty-fourth and forty-

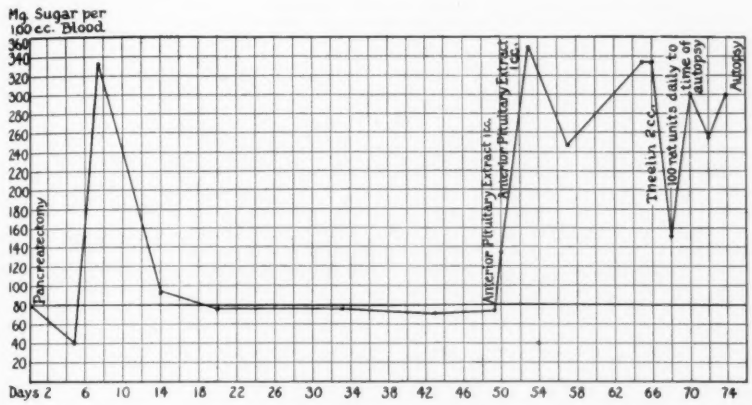


Fig. 5 (cat 65).—Blood sugar determinations in a cat which twenty-six days previous to pancreatectomy had received a lesion of the hypothalamus. Injections of an anterior lobe extract subsequent to pancreatectomy produced a hyperglycemia which injections of theelin did not lower.

fifth days, 1 cc. of an anterior lobe extract was injected intramuscularly. Glycosuria developed immediately and the blood sugar reading was 350 mg. on the forty-eighth day. With one exception of 246 mg., the blood sugar level was between 300 and 350 mg. following the injection of the anterior lobe extract until the time of death, and glycosuria was constantly present. Despite the hyperglycemia and glycosuria the cat remained active and alert, although it lost weight slowly. The animal was killed on the seventy-fourth day. Injection of 100 rat units of theelin each day during the last nine days did not lower the blood sugar or decrease the glycosuria (fig. 5).

Pathologic Anatomy.—The lesions were situated in the tip of the tuber cinereum at the level of the beginning of the infundibulum, just dorsolateral to the pars tuberalis of the hypophysis. The right wall of the third ventricle was damaged by the needle puncture and the right ventral periventricular nucleus was destroyed. Both ventromedial hypothalamic nuclei were destroyed and the left dorsomedial nucleus was damaged. The tangential and filiform nuclei were intact. The third

ventricle was slightly dilated. The hypophysis was intact. The lesions were restricted and did not extend as far caudad as the postinfundibular recess (fig. 6).

A small amount of fat and some lymphoid and connective tissue were observed in this animal's abdomen, together with a small group of minute nodules containing what closely resembled ducts or alveoli. Each nodule was separate and surrounded by dense connective tissue. The group was partially invested by lymphoid tissue.

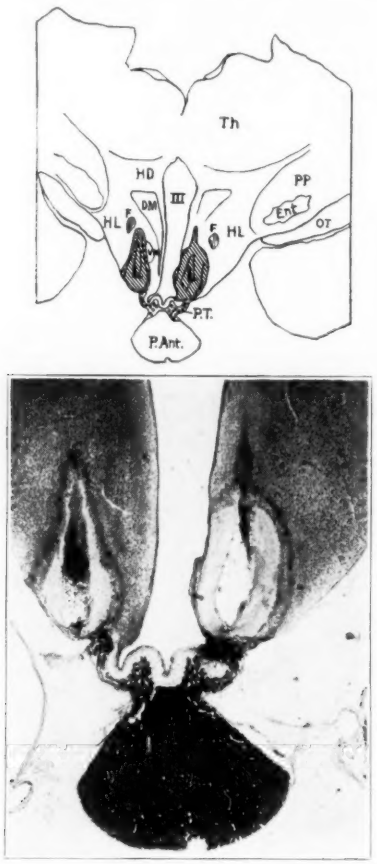


Fig. 6 (cat 65).—Bilateral lesions of the hypothalamus. *VM* represents the nucleus hypothalamicus ventromedialis; *DM*, the nucleus hypothalamicus dorsomedialis, and *HD*, the dorsal hypothalamic area.

Some of the nodules presented a cellular arrangement suggesting islet tissue, but the staining intensity was different from that in normal pancreas and there was a scarcity of blood cells. Some of the cells had a swirling arrangement; some possessed elongated nuclei and others crescentic nuclei.

Cat 77.—A hypothalamic lesion was made on June 2, 1933; pancreatectomy was performed on July 15, and the animal was killed on August 1.

The blood sugar varied between 52 and 89 mg. for thirty-seven days following the lesion in the hypothalamus. On the thirty-eighth day the blood sugar was

100 mg. The pancreas was removed on the thirty-ninth day; four days later the blood sugar was 139 mg., although no insulin had been given. During these days slight glycosuria was present. From then on, with the exception of the eleventh and sixteenth days when the blood sugar was 163 and 350 mg., respectively, it remained between 110 and 130 mg. On both occasions when the blood sugar was high, the cat struggled unusually hard when the blood was withdrawn. The animal remained well and active until it was killed on the twenty-second day after the pancreatectomy (fig. 7).

Pathologic Anatomy.—The rather large, round lesions were situated dorso-caudal to and impinged on the optic chiasm somewhat symmetrically. The right lesion was farther lateral than the left and touched the optic tract and the medial

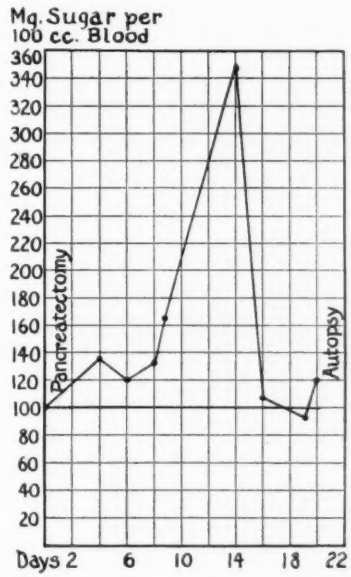


Fig. 7 (cat 77).—Blood sugar determinations in a cat which thirty-eight days previous to pancreatectomy had received a hypothalamic lesion.

edge of the entopeduncular nucleus. The left almost touched the nucleus ovoideus. On the right the lesion was extended dorsally by an area of softening, evidently of vascular origin, which extended into the dorsal thalamus. The subcommissural portion of the third ventricle was greatly dilated and the left needle puncture produced softening, indentation and destruction of the ependyma and periventricular system at that point. The left nucleus filiformis was completely destroyed; the vertical portion of the right was largely intact but the horizontal portion was destroyed. The anterior part of the left tangential (supra-optic) nucleus seemed pale and contained fewer cells than usual; its caudal part was slightly affected by the lesion directly and the remaining cells appeared pale. On the right, the anterior part of the tangential nucleus was largely destroyed; the medial portion remained intact and was of normal appearance. Its caudal segment was present but did not present a perfectly normal appearance. The anterior hypothalamic nucleus was completely destroyed on the left and almost completely on the right.

The left nucleus dorsomedialis and nucleus ventromedialis were destroyed along with the adjacent nucleus periventricularis. On the right the nucleus periventricularis and nucleus ventromedialis remained intact, while the nucleus dorsomedialis was partly damaged. The ventral nucleus periventricularis in the neighborhood of the infundibulum appeared to be largely missing. The right lateral hypothalamic area rostral to the nucleus subthalamicus was completely destroyed; the left was intact. The caudal part of the hypothalamus, including the mamillary bodies, appeared

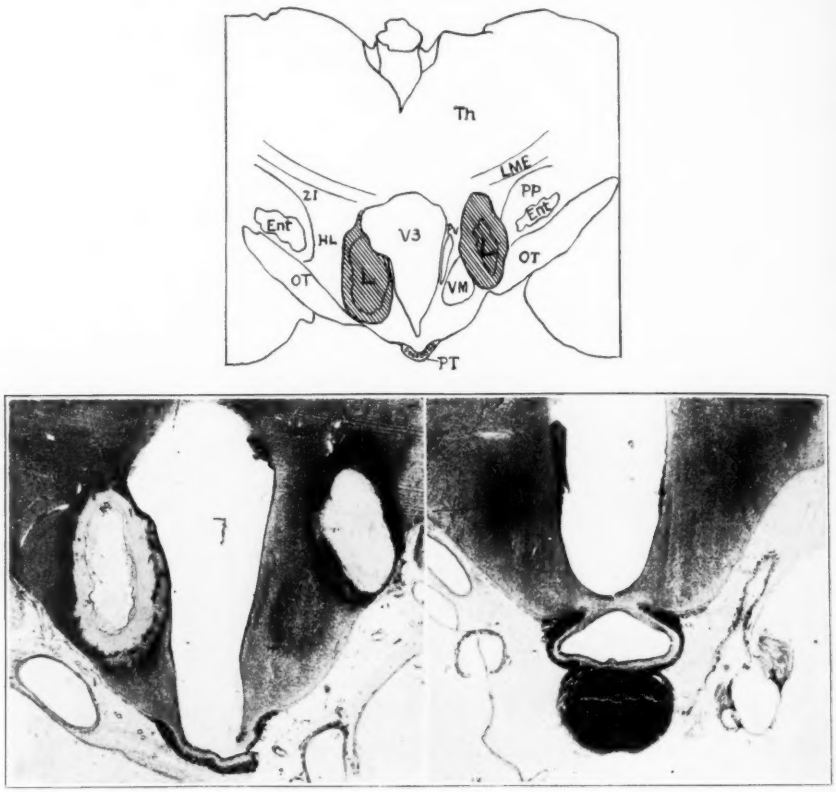


Fig. 8 (cat 77).—Bilateral lesions in the hypothalamus. *ZI* represents the zona incerta; *V3*, the third ventricle.

intact. The hypophysis was unharmed although the infundibulum was dilated. Both fornices were interrupted and largely degenerated. No fragments of tissue suggesting pancreatic tissue were observed either grossly or microscopically (fig. 8).

Comment.—In five cats in which lesions had been made with the Horsley-Clarke apparatus and the pancreas removed, hyperglycemia and glycosuria occurred as in a normal animal which has had its pancreas removed. These animals furnish some degree of negative evidence when studied in relation to the lesions which were observed to be present. The protocol of cat 83 may be given in detail and the others abstracted.

CAT 83.—A hypothalamic lesion was made on June 19, 1933; pancreatectomy was done on July 19 and 100 rat units of theelin given from July 21 to 29. The animal was killed on July 29.

Thirty-one days previous to pancreatectomy, single lesions were made on each side of the midline in the hypothalamus. On the fourth day of this period the blood sugar was 133 mg., but otherwise stayed between 68 and 100 mg. The first day following pancreatectomy the blood sugar rose to 334 mg., but dropped to 242 mg. on the seventh day. It then rose slowly to 300 mg. on the thirteenth day. It was 357 mg. at the time the animal was killed, on the fourteenth day. Although the blood sugar remained at a high level and glycosuria was present, in behavior and general appearance the animal was like the cats in the laboratory which had not been operated on. One hundred rat units of theelin was injected intramuscularly each day following the pancreatectomy in an attempt to depress the function of the hypophysis (fig. 9).

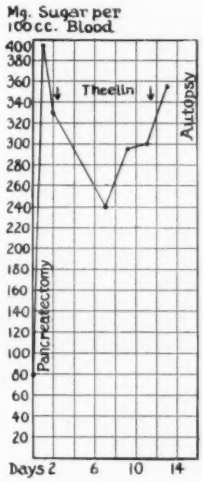


Fig. 9 (cat 83).—Blood sugar determinations in a cat which had received a hypothalamic lesion thirty days previous to a pancreatectomy, followed by the administration of theelin.

Pathologic Anatomy.—The lesions were quite large, lying just caudal to the nucleus hypothalamicus ventromedialis, and destroying the walls of the dorsal two thirds of the subcommissural portion of the third ventricle at this level. Most of the caudal part of the tuber cinereum was destroyed over an area extending between the lateral hypothalamic areas, but a bit of tissue at the tip above the caudal part of the opening of the infundibulum and around the postinfundibular recess remained intact. The subcommissural portion of the third ventricle was somewhat dilated. The ventral part of the posterior hypothalamic area was somewhat damaged, the effect of the lesions extending into the rostral poles of the mamillary bodies, although the bulk of the latter remained intact. The left fornix was interrupted, the right only partly destroyed. The filiform nuclei and rostral portions of the tangential nuclei apparently were intact and somewhat less well developed than usual. The anterior hypothalamic nuclei and the dorsomedial and ventromedial nuclei were intact as far caudally as the posterior pole of the ventromedial nucleus,

which marked the rostral limit of the lesion. The hypophysis was intact. No fragment resembling pancreatic tissue was seen (fig. 10).

In cat 13, the lesion affected the structures to the left of the midline only and extended from the optic chiasm to the posterior margin of the infundibular opening. On the left the nucleus ovoideus, nucleus ventromedialis, nucleus dorsomedialis and nucleus periventricularis ventralis were damaged severely or destroyed completely. The left nucleus filiformis and nucleus tangentialis pars caudalis were slightly injured. The left angle of the infundibulum and adjacent pars tuberalis

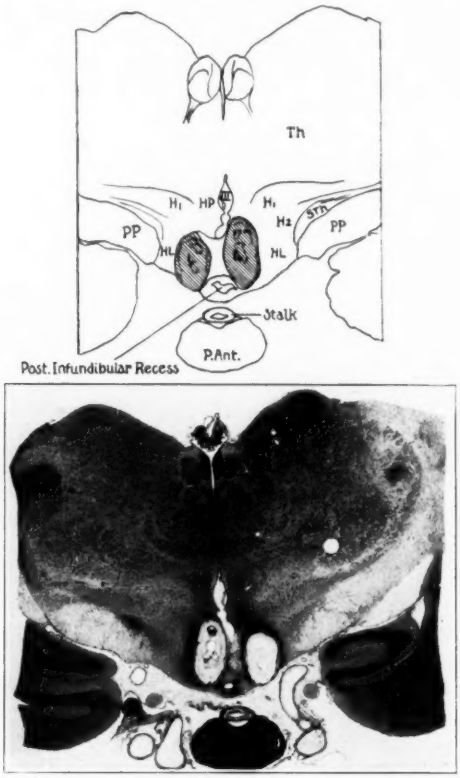


Fig. 10 (cat 83).—Bilateral lesions of the hypothalamus.

were damaged. The left margin of the pars anterior of the hypophysis was also affected with the involvement of perhaps less than one quarter of the lobe.

In cat 60, the lesions were restricted but unsymmetrical. The lesion on the right side affected the lateral hypothalamic area chiefly; that on the left, the region of the nucleus ventromedialis. The supra-optic group of nuclei were intact and the hypophysis was undamaged.

In cat 67, little damage was done to either the hypothalamus or the hypophysis. The lesions affected chiefly the meninges lateral to the infundibulum. The left nucleus ventromedialis was injured slightly and the rest of the damage was confined to the ventral surface of the tuber cinereum just caudolateral to the opening of the infundibulum. The hypophysis was uninjured.

The lesions were seen to be displaced to the right in cat 70. One lesion was in the midline, the other in the lateral hypothalamic area. The latter lesion produced some injury to the right ventromedial nucleus. The left lesion affected chiefly a small area about the postinfundibular recess just caudal to the opening of the infundibulum, and extended caudad to involve the mamillary bodies. The tangential nucleus was intact, as was the left filiform nucleus. There was some doubt as to the integrity of the right filiform nucleus. The subcommissural portion of the third ventricle was dilated markedly. The hypophysis was intact.

COMMENT

As has been noted by Ingram,[10] destructive lesions of the hypothalamus in cats are followed by a temporary rise in blood sugar which later falls to normal. Likewise irritative lesions of the hypothalamus produce an increase in blood sugar but no polyuria. Our animals showed such a rise, which gradually disappeared. Each of the animals also had hyperglycemia and glycosuria immediately following removal of the pancreas. It was thought necessary in several instances to give insulin to tide the animal over this initial period. This was not done in cat 77, and the blood sugar returned to normal as quickly as in the other animals which were treated.

In cat 65, anterior lobe extract was injected intramuscularly on two days after the blood sugar had remained between 70 and 75 mg. for twenty days. Glycosuria and hyperglycemia immediately resulted and persisted. On the basis of the assumption that theelin depresses the function of the pituitary gland, this was given in an effort to counteract the effect of the anterior lobe extract, but it was without result. It is difficult to offer any logical explanation for the effect of anterior lobe extract in this instance, and we have not as yet had the opportunity of repeating the experiment on a sufficiently large group of animals.

The sympathetic innervation of the posterior pituitary lobe by way of the carotid plexus is known to be scanty, but its nerve supply is massive via the tractus hypothalamicohypophyseus, which arises from numerous hypothalamic nuclei but chiefly from the supra-optic or tangential nucleus and runs down the stalk. This tract theoretically should have been interrupted or severely damaged in cat 13, but in none of the others was it affected to any extent. Interruption of this tract has been found to produce marked and permanent polyuria. The origin of the fibers innervating the anterior pituitary lobe has never been determined. It is logical to assume, in view of considerable earlier work, that they may directly or indirectly arise in some region of the hypothalamus. Lesions in these regions, which must be bilateral, would have the effect of at least partially denervating the anterior lobe. It is

10. Ingram, W. R.: Personal communication to the authors.

interesting to note that the lesions in cats which survived pancreatectomy had the point in common that they were placed so as to involve the region of the fornix and affect the perifornical nuclei. Such lesions must be situated in the tuber cinereum slightly rostrodorsolateral to the mamillary bodies. It is at about this level that the ventromedial hypothalamic nucleus lies. The lesions in cats which did not survive pancreatectomy did not seriously affect this region, or left it entirely unscathed on one side of the hypothalamus. In cat 83 which survived pancreatectomy in good condition for fourteen days although having a high blood sugar, the lesions were placed so as to involve completely this region on one side, but only partly to affect it on the other. It is also interesting that in animals in which Ranson, Magoun and Barris [11] found an elevation of blood sugar from faradic stimulation of the hypothalamus, the foci of stimulation were found to lie in the neighborhood of the fornix and perifornical nuclei.

The evidence regarding the neural mechanisms involved is definitely anatomic in character. In 1913 Dandy [12] demonstrated sympathetic nerve fibers which spread from the carotid plexus, coursing along the vessels of the stalk, to the anterior lobe of the hypophysis. Nonmyelinated fibers, first described by Cajal,[13] have been traced more recently by Greving [14] and Pines [15] from both the supra-optic and the periventricular nuclei to ramify through the pars nervosa. Kary [16] and Lewy [17] have reported retrograde changes in the cells of the nucleus supra-opticus and the tuberal nuclei after injury to the posterior lobe of the dog's pituitary gland. With knowledge at hand concerning the abundant nerve supply from the hypothalamus to the pituitary body, one cannot entirely ignore consideration of the results which follow interruption of these neural connections.

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11. Ranson, S. W.; Magoun, H. W., and Barris, R. W.: Stimulation of the Hypothalamus with the Horsley-Clarke Stereotaxic Instrument, Anat. Rec. **52**:24, 1932.

12. Dandy, W. E.: The Nerve Supply to the Pituitary Body, Am. J. Anat. **15**:333, 1913.

13. Ramón y Cajal, S., quoted by Cushing.[4]

14. Greving, R.: Beitrage zur Anatomie der Hypophyse und ihrer Funktion, Deutsche Ztschr. f. Nervenh. **88-89**:179, 1925; Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:466, 1926.

15. Pines, I. L.: Ueber die Innervation der Hypophysis cerebri, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:123, 1926.

16. Kary, C.: Pathologisch-anatomische und experimentelle Untersuchungen zur Frage des Diabetes insipidus und der Beziehungen zwischen Tuber Cinereum und Hypophyse, Virchows Arch. f. path. Anat. **252**:734, 1924.

17. Lewy, F. H.: Infundibulare Veränderungen beim Diabetes insipidus und die Beziehungen zwischen Tuber Cinereum und Hypophyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **37**:398, 1924.

Some years ago, Dandy and Goetsch [18] gave a detailed account of the main sources of the arterial blood supply of the canine pituitary gland. Recently Popa and Fielding [19] have shown in the human pituitary gland that the blood from the anterior and posterior lobes is not drained entirely into the basilar circle of veins which overlie the circle of Willis, but that a large amount of it passes upward through a number of parallel veins into the tuber cinereum. These vessels ramify in relation to the nuclei of this region and have been called hypophyseoportal veins. Basir [20] has stated also that these long vessels run beneath the ependyma of the third ventricle, where they form an arched capillary plexus without being enclosed in perivascular spaces such as the systemic vessels have. The hypothalamic nuclei are supplied by systemic vessels from the circle of Willis and by the hypophyseoportal veins.

It is conceivable that these hypothalamic lesions interrupted the nerve pathways just described to the hypophysis, or seriously interfered with its blood supply. Any definite conclusions regarding these two points must await further evidence.

EFFECT OF STIMULATION OF THE AUTONOMIC NERVOUS SYSTEM

In an effort to prove whether or not stimulation of the sympathetic fibers which Dandy had demonstrated as coursing from the carotid plexus to the anterior lobe had an effect on the hypophysis, Weed, Cushing and Jacobson [2] stimulated the superior cervical sympathetic ganglion in rabbits, cats and dogs. They found that, provided the animal had available glycogen stored up, glycosuria invariably resulted. At that time they had no dependable methods for testing blood sugar. Glycosuria resulted even after section of the vagi and transection of the spinal cord at the level of the fourth thoracic segment. On the other hand, stimulation of the sympathetic chain did not produce glycosuria. After removal of the posterior lobe of the hypophysis, stimulation of the ganglion did not produce glycosuria. Direct stimulation of the hypophysis was followed by glycosuria even after transection of the spinal cord.

They concluded that the glycosuria which followed stimulation of the superior cervical ganglion was due not to a nerve reflex but to a chemical stimulus to glycogenolysis arising somewhere in the cephalic course of the cervical sympathetic fibers. They believed that the chemical

18. Dandy, W. E., and Goetsch, E.: The Blood Supply of the Pituitary Gland, Am. J. Anat. **2**:137, 1911.

19. Popa, G. T., and Fielding, U.: A Portal Circulation from the Pituitary to the Hypothalamic Region, J. Anat. **65**:88, 1930.

20. Basir, M. A.: The Vascular Supply of the Pituitary Body in the Dog, J. Anat. **66**:387, 1932.

substance discharged is carried through the vascular system to the storehouses for glycogen in the liver and muscles where it inaugurates glycogenolysis.

Shamoff [21] corroborated the production of glycosuria following stimulation of the superior cervical sympathetic ganglion but stressed the frequent occurrence of polyuria, which resembled that produced by the intravenous injection of extracts of the pituitary body. Keeton and Becht [22] stimulated the hypophysis directly in dogs and obtained results corroborative of those obtained by Cushing and his co-workers. When the splanchnic nerves were sectioned this result was not obtained. Keeton and Becht believed that their experiments spoke against the liberation of a hormone which caused the hyperglycemia. However, this does not follow necessarily, and, as they suggested, the site of the action of the hormone might be some central glycogenic center which requires an intact nerve pathway to the viscera for its discharge.

As Cushing has stated, his experiments may be capable of reinterpretation in the light of new knowledge. It appeared to us that a series of experiments based on that work might be undertaken which would supply some evidence on the relation of the hypophysis, its autonomic nerve supply, the hypothalamus regarded as a higher sympathetic nerve center and carbohydrate metabolism.

Stimulation of the Superior Cervical Sympathetic Ganglion.—The superior cervical sympathetic trunk and ganglion were dissected free from the vagus nerve and a piece of rubber dam was placed about the ganglion to prevent a spread of current. Faradic stimulations, with the secondary coil set at 8 cm., were used throughout the entire series of stimulation experiments. Three stimulations, each of thirty seconds' duration, with intervals of two minutes between each, were employed. Readings of blood sugar were made on each animal before the experiments began. Female cats were used, and specimens of urine were collected by catheterization of the bladder. Pentobarbital-sodium, 0.5 cc. per kilogram of body weight, and sodium amytal, 0.5 cc. per kilogram of body weight, were used intravenously for anesthesia. In five control cats anesthetized with pentobarbital-sodium and in four animals to which sodium amytal was given, glycosuria did not develop and the readings of the blood sugar did not rise above 150 mg., which is considered the upper normal level in anesthetized cats.

Seven animals were used in this experiment. In five the average initial blood sugar was 104 mg. per hundred cubic centimeters of blood; the average final blood sugar taken after the stimulations were made was 251 mg., and the median final blood sugar, 294 mg. (fig. 11). Three animals showed heavy glycosuria, one moderate and one slight. The flow of urine was increased, and the color and specific gravity became lighter. In two animals which were not fed for forty-eight

21. Shamoff, V. N.: On the Secretory Discharge of the Pituitary Body Produced by Stimulation of the Superior Cervical Sympathetic Ganglion, Am. J. Physiol. **39**:279, 1916.

22. Keeton, R. W., and Becht, F. C.: The Stimulation of the Hypophysis in Dogs, Am. J. Physiol. **39**:109, 1916.

hours previous to stimulation, the blood sugar determinations were vitiated by deteriorated chemicals. No glycosuria followed the stimulations, although the flow of urine was increased and its color became lighter.

Stimulation of the Stellate Ganglion.—In four animals the stellate ganglion was stimulated after exposure by the posterior thoracic operation and its isolation by a rubber dam. The average initial blood sugar was 102 mg.; the average and median final blood sugar, 324 mg. Three of these cats showed moderate glycosuria and the other heavy glycosuria. The flow of urine was increased slightly and its color became lighter.

In four other cats, the sympathetic trunk was cut below the stellate ganglion before the stimulations were carried out. In these animals the average initial blood sugar was 114 mg.; the average final determination was 213 mg. and the median final value 222 mg. One cat had moderate glycosuria; two showed slight glyco-

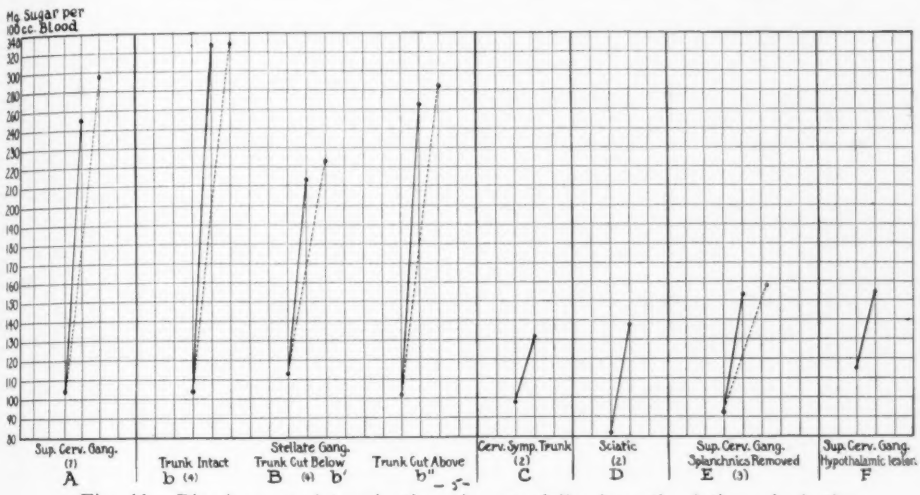
Mg. Sugar per 100 cc. Blood
Sup. Cerv. Gang. (7) A
Trunk Intact b (4)
Stellate Gang. Trunk Cut Below B (4) b'
Trunk Cut Above b''
Cerv. Symp. Trunk (2) C
Sciatic (2) D
Sup. Cerv. Gang. Splanchnics Removed E (3)
Sup. Cerv. Gang. Hypothalamic lesion. F

Fig. 11.—Blood sugar determinations in cats following stimulation of *A*, the superior cervical sympathetic ganglion; *B*, the stellate ganglion when (*b*) the sympathetic trunk was intact, (*b'*) the trunk was cut below the ganglion and (*b''*) the trunk was cut above the ganglion; *C*, the cervical sympathetic trunk; *D*, the sciatic nerve; *E*, the superior cervical sympathetic ganglion with the splanchnic nerves removed, and *F*, the superior cervical sympathetic ganglion following a hypothalamic lesion. In these graphs solid lines indicate the average final blood sugar level following stimulation; dotted lines, the median final blood sugar. Numerals represent the number of cats used in the experiments.

suria, and the other animal had only a trace of sugar in the urine. There was only moderate increase in the flow of urine, but the color became lighter.

In five animals the sympathetic trunk was cut above the stellate ganglion, after which the ganglion was stimulated. The average initial blood sugar was 104 mg. and the average and median final determinations 264 and 286 mg., respectively. Two of these cats showed no glycosuria and the other three had a moderate positive reaction. The flow of urine was increased moderately and the color became lighter (fig. 11).

Stimulation of the Cervical Sympathetic Trunk.—In two cats the cervical sympathetic trunk was stimulated. No glycosuria developed, and the blood sugar

rose from an average of 98 to 132 mg., both of which readings are entirely within normal limits (fig. 11).

Stimulation of the Sciatic Nerve.—As a control experiment the sciatic nerve was stimulated in two animals. Glycosuria did not develop, and the average initial blood sugar level of 81 mg. rose to 139 mg. Again these readings are within normal limits (fig. 11).

Stimulation of the Superior Cervical Sympathetic Ganglion After Removal of the Splanchnic Nerves.—In three cats the splanchnic nerves were removed on both sides by a subdiaphragmatic approach. Ten days later the superior cervical sympathetic ganglion was stimulated. Glycosuria did not develop and the average initial blood sugar level of 91 mg. rose to a final level of 152 mg., which is within normal limits (fig. 11).

Stimulation of the Superior Cervical Sympathetic Ganglion After a Lesion of the Hypothalamus.—In three cats a hypothalamic lesion was made from two to three weeks before stimulation of the superior cervical sympathetic ganglion was carried out. The preliminary rise in blood sugar which follows these lesions immediately had returned to normal. In two cats the average initial blood sugar determination was 106 mg., and the average final reading was 145 mg. There was no glycosuria, and a very slight increase in the flow of urine was noted. In one cat, the initial blood sugar level was 115 mg., which rose to 200 mg. after the stimulation. The urine showed a heavy reaction for sugar (fig. 11). The protocols of these experiments are as follows: [23]

CAT 31.—On Oct. 28, 1933, stimulation of the right superior cervical sympathetic ganglion raised the blood sugar level to 273 mg. Marked glycosuria was present. On December 28, bilateral lesions were made in the hypothalamus. On Jan. 12, 1934, at which time the blood sugar was 113 mg., the left superior cervical sympathetic ganglion was stimulated. The blood sugar rose to 165 mg., and the urine did not reduce Benedict's solution.

CAT 57.—The blood sugar was 93.5 mg. on Jan. 23, 1934, when bilateral hypothalamic lesions were made. The right superior cervical sympathetic ganglion was stimulated on February 13. The initial blood sugar was 100 mg., and after stimulation rose to 125 mg. No glycosuria occurred.

CAT 3.—The initial blood sugar was 107 mg. Following stimulation of the right superior cervical ganglion it rose to 376 mg. and there was heavy glycosuria. Bilateral hypothalamic lesions were made on November 11. On December 28, the blood sugar was 115 mg. The left superior cervical sympathetic ganglion was stimulated; the blood sugar rose to 200 mg., and glycosuria was present.

The pathologic changes noted in these animals were as follows:

In cat 31 the puncture marks were asymmetrical, one almost in the midline and the other to the left of it. The lesions were just caudal to the ventromedial hypothalamic nuclei, caudal to the beginning of the stalk of the pituitary body and just rostral to the mamillary bodies, damaging the rostral poles of the latter. Thus the ventral part of the posterior hypothalamic area and the premamillary areas were affected, with some damage to the ventral parts of the walls of the third ventricle at this point. On the right the fornix and its surroundings were

23. All of these animals were fed 80 cc. of canned milk, 10 cc. of hepatin and 50 grains (3.2 Gm.) of chopped beef heart the day before the final stimulations were made. They had been eating normally, but we wished to insure available glycogen.

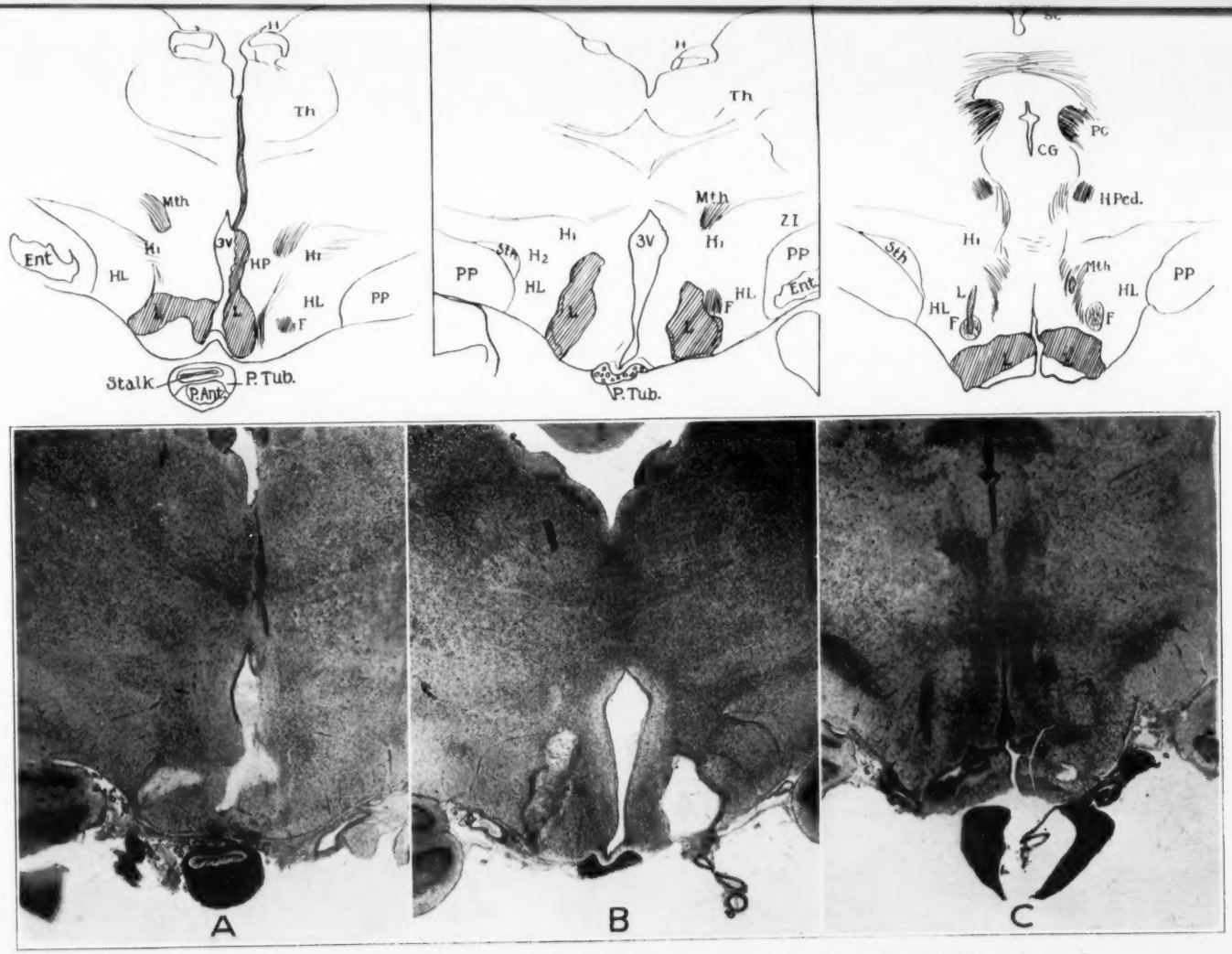

Fig. 12 (cats 31, 57 and 3).—Lesions in the hypothalamus: *A*, in cat 31; *B* in cat 57; *C*, in cat 3.

intact. On the left the lesion extended laterad to the medial edge of the medial bundle of the forebrain, destroying the fornix just before its entrance into the mamillary bodies. The rostral portion of the supramamillary area was damaged.

In cat 57 the lesions were not quite symmetrical, and on the left there was a small hemorrhage elongating the lesion dorsoventrally. The lesions damaged severely the caudal portions of the ventromedial nuclei and extended caudad as far as the premamillary area at the ventral surface of the hypothalamus. The lateral hypothalamic areas were not significantly affected. The left fornical region was destroyed; on the right the fornix itself was slightly affected, the medial perifornical region being destroyed. There was no damage to the stalk or hypophysis.

In cat 3 the lesion could be seen in sections stained with Weil's method, but on account of a peculiar slant to the sections and because the pituitary gland and its stalk were torn away, thus damaging the tuber, exact localization was difficult. A good view of the lesion was had in sections stained with cresyl violet. The location of the lesion here was similar to that in cat 31, but it was more symmetrical. It seemed to lie just rostral to the mamillary bodies, slightly damaging the latter. There was considerable damage to the ventrocaudal part of the tuber at the ventral surface of the brain in the premamillary region. The fornices were hardly affected, the left only by the passage of the needle; both were more directly damaged close to the mamillary bodies, but they showed no retrograde degeneration.

In cats 31, 57 and 3 the lesions were situated very near the ventral surface of the hypothalamus, those in cat 57 lying somewhat farther rostrad. The exact extent of injury in cat 3 was difficult to determine owing to the fact that the hypophysis was torn away at autopsy, with consequent damage to the tuber cinereum. However, in the latter case the lesion affected chiefly a restricted area immediately rostral to the mamillary bodies, with some damage to these structures. In cat 31, the lesions affected a somewhat similar area but more injury was done to the walls of the third ventricle and the left perifornical area was destroyed. In cat 57 the lesions were more symmetrical and the perifornical areas were both damaged; on the left the latter was completely destroyed and on the right partially. Here the lesions bordered closely the lateral hypothalamic areas. It may be pointed out that in cat 31 the walls of the third ventricle were damaged sufficiently to suggest a possible interference with the action of hypophyseal substances on the hypothalamic nuclei. In cat 57 the symmetrical lesions might well have produced sufficient damage to the hypothalamic structures to have a similar effect. So far as can be determined, the lesions in cat 3 were not of a type that would necessarily act in such a manner. However, the material at hand at present is not sufficient to justify the drawing of positive conclusions.

COMMENT

The results of these experiments corroborate the earlier results of Weed, Cushing and Jacobson and add more conclusive evidence provided by blood sugar determinations, which were not available in 1913. Stimulation of the superior cervical sympathetic ganglion produces hyperglycemia and glycosuria, and this result may also be obtained by

stimulation of the stellate ganglion but not by stimulation of the cervical sympathetic trunk.[24] Division of the sympathetic trunk above or below the stellate ganglion reduced the strength of the response but did not abolish it. In addition we have shown that removal of the splanchnic nerves interferes with the production of hyperglycemia and glycosuria.

We are able to reemphasize an important point made by Cushing and his co-workers. Glycogen must be available before the metabolism of carbohydrates can be upset by stimulation of the sympathetic ganglion. We proved this to our own satisfaction in animals which had fasted from twenty-four to forty-eight hours. In these experiments repeated stimulations failed to raise the blood sugar level or cause sugar to spill over in the urine. Our animals were fed carefully and, in the event of there being a question about the amount of food taken, were given supplemental feedings by stomach tube. We were therefore sure at all times that the problem of feeding did not enter into our results.

Weed, Cushing and Jacobson were never able to make their animals sugar-free after attempts to remove the splanchnic nerves. Autopsies on our animals were done carefully to prove the complete section of these nerves as they entered the abdominal cavity through the diaphragm. None of our animals showed glycosuria or elevated blood sugar following this operation. Neither were we able to produce hyperglycemia or glycosuria in these animals by stimulation of the superior cervical sympathetic ganglion. Though we have not as yet repeated the work of these investigators with reference to transection of the spinal cord, it is possible that section at the level of the fourth thoracic segment did not remove the possibility of origin of the splanchnic nerves from the uppermost thoracic segments of the cord as some investigators have maintained.

A lesion of the hypothalamus which destroyed certain definite nuclei or nerve pathways abolished the production of glycosuria and hyperglycemia after stimulation of the superior cervical sympathetic ganglion. One might argue that the hypophysis is stimulated by impulses reaching it over fibers from the superior cervical sympathetic ganglion with synapses in the hypothalamic nuclei, and that its secretion is then thrown into the blood stream and produces its effects on the glycogen storehouses in the body. The difference between the rise of the blood sugar following stimulation of the superior cervical sympathetic ganglion with the hypophysis and hypothalamus intact and that which occurred in these animals with a hypothalamic lesion is striking.

24. This is analogous to the observations on the production of pain by stimulation of the superior cervical sympathetic ganglion and chain which Pollock and Davis made on animals.

Griffith [25] reported experiments which show that reflex stimulation of the vagus, crural or sciatic nerves may increase the blood sugar. He believed that there is no doubt that this form of hyperglycemia is independent of the activity of the glycosecretory nerves to the liver, but that it is due to reflexly stimulated activity of the suprarenals. Likewise he stated that certain other experiments indicate that the pancreas, thyroid, parathyroid and hypophysis are not involved in the development of this hyperglycemia which occurs from vagal or sciatic stimulation if the suprarenals are intact. He assumed, but with the question evidently open in his mind, that the hypophysis is denervated by section of both cervical sympathetic trunks. Houssay, Biasotti and Rietti [3] recently reported that the diabetogenic action of anterior lobe extract may be observed in the absence of the pancreas, hypophysis, thyroid, ovaries, testes, splanchnic nerves, lumbar sympathetic chains or suprarenals or with a lesion of the tuber cinereum. They concluded that the liver alone was necessary. Mainly as the result of experiments with the transplanted pancreas in pancreatectomized animals, it has been suggested that nerve impulses to the pancreas are of little importance for the regulation of blood sugar. Though the nerve supply may not be absolutely necessary for the function of the pancreatic islets, it does not necessarily follow that the regulation of the secretion of insulin may not be under the control of nerve impulses.

We have no evidence which would lead to any information regarding the source of the carbohydrates mobilized in these experiments. Griffith's experiments would seem to rule out the glycosecretory nerves of the liver. This would then leave, as he has indicated, increased flow of blood through the liver, glycosecretory nerves to the muscles and concentration of the blood in some manner as yet unknown.

SUMMARY

Hyperglycemia and glycosuria are not produced by pancreatectomy in cats which have a lesion of the hypophysis.

Bilateral hypothalamic lesions, symmetrically placed, may be followed by pancreatectomy without the development of hyperglycemia and glycosuria. Such lesions must be situated in the tuber cinereum slightly rostrodorsolateral to the mamillary bodies at the level of the ventromedial hypothalamic nucleus.

Stimulation of the superior cervical sympathetic ganglion and the stellate ganglion in cats produces marked hyperglycemia and glycosuria. These results are not obtained following section of the splanchnic nerves or bilateral, symmetrical lesions of the hypothalamus.

25. Griffith, F. L.: Reflex Hyperglycemia: A Study of the Carbohydrate Mobilization Effected by Afferent Crural, Sciatic and Vagus Stimulation, Am. J. Physiol. **66**:618, 1923.

DISCUSSION

DR. S. W. RANSON, Chicago: The large bilaterally symmetrical lesions which were so beautifully shown in Dr. Davis' slides must, I am sure, have aroused interest. It is certain that the Horsley-Clarke machine makes it possible to place lesions in the deeper part of the brain with a precision which otherwise cannot be attained. It is difficult to understand why it has been used so little in the past twenty years.

There is, as is generally known, the closest possible relationship between the hypothalamus and the hypophysis. Topographically, they lie close together, connected by the infundibulum. Tumors in one structure are likely to press on the other, and in experimental work it is difficult to place lesions in either region without damaging the other. If the tuber cinereum is approached by raising the brain, it is impossible to avoid traction on the infudibulum and there is the possibility that damage may be done to the stalk and the blood and nerve supply of the hypophysis.

The hypothalamus sends a bundle of nerve fibers, the tractus hypothalamicohypophyseus, to the posterior lobe of the hypophysis from which fibers extend to the pars intermedia. Through this tract the hypothalamus is in a position to influence the functions of the hypophysis. It is generally believed that hormones formed in the hypophysis may make their way directly to the hypothalamus, either by way of the portal type of circulation described by Popa and Fielding or by direct transmission through the stalk into the cavity of the infundibulum and the third ventricle. If this is true, hypophyseal hormones may exert an important regulatory influence over hypothalamic function. In view of the close topographic neural and hormonal relations which exist between the two structures, it is not surprising that the greatest confusion exists as to which functions are properly assignable to the hypothalamus and which to the hypophysis. Obviously, some functions may depend on the integrity of the joint hypothalamicohypophyseal mechanism.

The confusion and contradiction which exist in the literature on this subject show the need of new methods of study, of which one is furnished by the Horsley-Clarke apparatus. By its use it is possible to place bilaterally symmetrical lesions in any part of the hypothalamus desired without damage to the stalk or to the blood supply of the hypophysis or pars tuberalis. The lesion can at will be placed so as to interrupt or to leave intact the hypothalamicohypophyseal tract. The method has great possibilities which are only just beginning to be realized.

Clinical Notes

A SIMPLE ROUTINE PROCEDURE FOR STAINING THE NEURONS AND GLIA OF THE NERVOUS SYSTEM

ELMER H. LOUGHLIN, M.D., BROOKLYN

A great step forward in the study of the elements of the nervous system and their pathologic alterations was made by the Spanish school of histologists, particularly Ramón y Cajal[1] and del Rio Hortega,[2] with the introduction of the gold and silver methods now in use. Because they necessitate the use of fresh material in small sections for the proper penetration of special and diverse fixatives and the staining of the tissues within short prescribed periods of time, difficulties are encountered, excellent as these methods are. Since it is often impossible to fix the nerve tissue shortly after death and it is frequently advantageous to study the hardened brain grossly before sectioning is undertaken, a routine fixative must be used which will meet these requirements. Not only are special fixatives required, but numerous stains are necessary to complete a satisfactory study of the tissues. In addition, many times, during routine sectioning of a hardened brain, a tumor is encountered. If the tumor has not been especially fixed, it becomes extremely difficult or impossible to stain.

To overcome some of these difficulties, Globus,[3] in 1927, introduced ammonia and hydrobromic acid as rejuvenating agents in the preparation of formaldehyde-fixed material for the Cajal and Hortega staining procedures. He believed that the cells in old formaldehyde-fixed tissues became so altered that the metals could not penetrate, but would only plate the surfaces.[4] The results with the new step, although sometimes good, are not uniform, the Cajal preparations in particular appearing granular and at times indistinct. Then, too, it is impossible with this modification to stain satisfactorily neoplasms composed of embryonic cells.

Formaldehyde is a fixative used as a routine procedure in the operating and postmortem rooms. It penetrates fairly rapidly and affords excellent fixation of tissue, besides being valuable as a preservative and relatively inexpensive. Thus, a staining procedure which would give uniformly good results with formaldehyde-fixed material would be the desired goal.

From the Department of Pathology, Long Island College of Medicine.

1. Ramón y Cajal, S.: Trab. lab. biol. invest. Univ. Madrid **11**:219, 1913; **14**:155, 1916.

2. del Rio Hortega, P.: Trab. lab. biol. invest. Univ. Madrid 1918, vol. 15; 1926, vol. 16; cited by Globus.[3]

3. Globus, J. H.: The Cajal and Hortega Glia Staining Methods, Arch. Neurol. & Psychiat. **18**:263 (Aug.) 1927.

4. Freeman, W.: Textbook of Neuropathology, Philadelphia, W. B. Saunders Company, 1933.

Having used the aforementioned methods and modification with frequent unsatisfactory results, owing to their vagaries or the "unsuitability" of the tissues, I attempted to develop a staining procedure which would give uniformly good results with formaldehyde-fixed material and so-called unsuitable tissue. While attempting unsuccessfully with the usual methods to stain the tissues of a child, aged 7 days (material from a rhinencephalocele that had not been fixed until several days post mortem and had been preserved in formaldehyde for three years), this method was conceived.

MATERIAL AND TECHNIC

The technic utilizes essentially Cajal's gold sublimate and Bielschowsky's [5] ammoniacal silver solutions in one procedure. The best features of each original method are retained, and both the neurons and the glia are demonstrated with a brilliance that I have never obtained by either method alone. However, instead of using hydrobromic acid as a mordanting agent, I employed dilute bromine water, since not only does it aid in yielding uniform results, but hydrobromic acid, as it ages, decomposes largely into this element.

To prove the efficacy of the method I used the most unsuitable tissues I could obtain, along with routine autopsy and operative material. Old formaldehyde-fixed material, tissue fixed in Zenker's solution, material that had not been fixed until several days post mortem in frozen, paraffin and pyroxyline (celloidin) sections, all were used with invariably good results.

Thin sections may be used, which, because of their greater clarity and the contrast of the elements with the background together with sharp definition, are most suitable for photographic representation.

As an additional feature, with this method the narrow time limits demanded previously have been eliminated for the most part. Also with this staining procedure, being useful in demonstrating most of the elements and their pathologic changes, the number of methods necessary to study a given piece of tissue has been cut down considerably.

The procedure is simple, and with fairly close adherence to the technic to be described, a technician not particularly versed in gold and silver staining methods will obtain remarkably good results.

Details of Technic.—1. Formaldehyde-fixed tissues are cut at from 15 to 18 microns; frozen sections are preferable because of ease in handling.

2. Rinse in distilled water and transfer to 5 per cent ammonia water overnight to remove the formaldehyde.

3. Place the sections directly in 2 per cent bromine water and allow to remain for from six to twenty-four hours.

4. Wash three times in distilled water.

5. Transfer into the following solution for from forty-eight to seventy-two hours: gold chloride (acid brown) 1 per cent, 10 cc.; corrosive mercuric chloride, 1 Gm., and distilled water, 60 cc. (dissolve the mercuric chloride in 20 cc. of distilled water with the aid of heat; add 10 cc. of gold chloride solution, and distilled water to 70 cc.). Place in the dark on top of an oven at 38 C.

6. Wash rapidly twice in distilled water.

5. Bielschowsky, M.: Jahrb. f. Psychol. u. Neurol. **3**:169, 1904; **12**:135, 1908.

7. Transfer to the ammoniacal silver solution, consisting of silver nitrate, 2 per cent, 60 cc., and sodium hydroxide, 40 per cent, 9 drops (dissolve the precipitate in strong aqua ammoniae, drop by drop, leaving a little precipitate undissolved at the end to insure against an excess of ammonia). Stain for from eight to ten minutes.

8. Wash rapidly, but thoroughly, once in distilled water.

9. Reduce in neutral solution of formaldehyde (1:5) in tap water for from one-half to one hour.

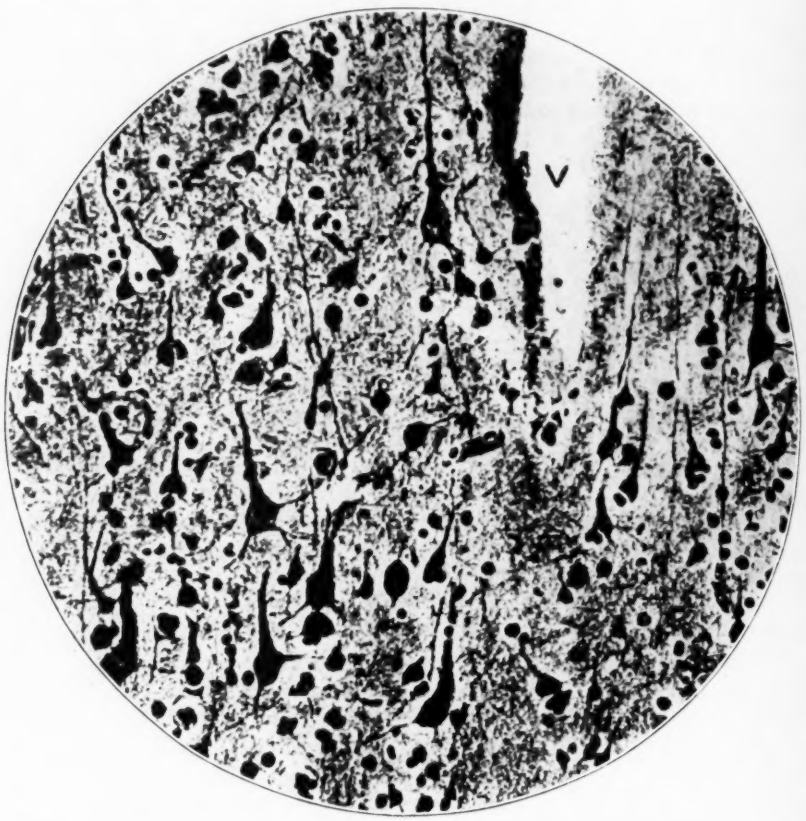

Fig. 1.—An area of cerebral cortex, in the vicinity of a tumor, showing degenerating ganglion cells. With a hand lens many oligodendroglia with their processes are visible. V indicates a blood vessel. The tissue is from a case brought to autopsy twenty-four hours post mortem and was preserved in a solution of formaldehyde for six years.

10. Wash rapidly in two changes of distilled water.

11. Tone in 0.5 per cent acid yellow gold chloride, made alkaline with from 1 to 2 cc. of a saturated solution of lithium carbonate or a few drops of 5 per cent sodium carbonate solution, for fifteen minutes.

12. Wash rapidly in one change of distilled water.

13. Fix in the following solution for five minutes: 5 per cent sodium thiosulphate, 40 cc., and 95 per cent alcohol, 10 cc.

14. Dehydrate in graded solutions of alcohol (25, 50 and 95 per cent), leaving the tissue in the last until the water is completely extracted.

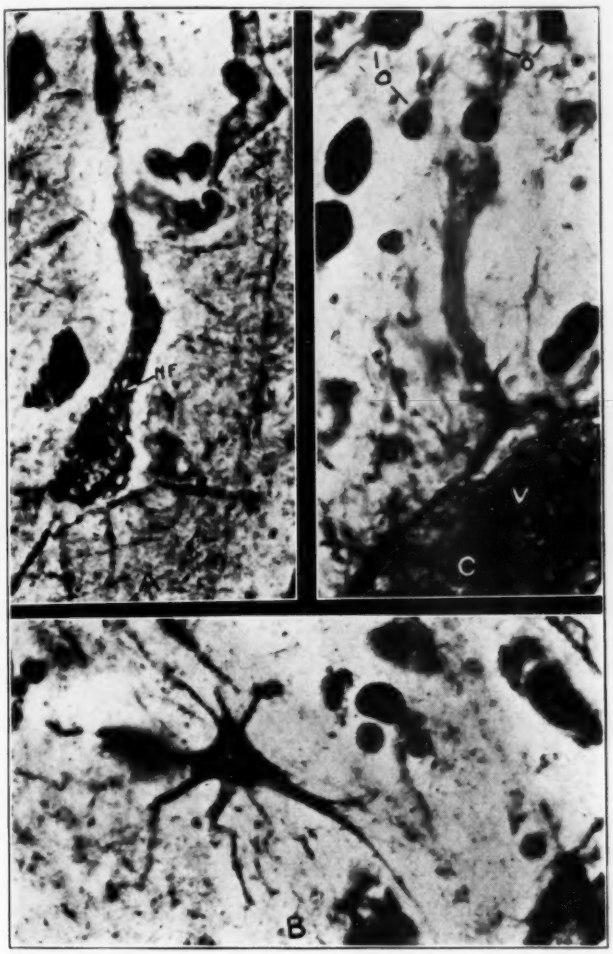

Fig. 2.—*A*, a degenerating ganglion cell in an area similar to that shown in fig. 1. Note the eccentric nucleus with nucleolus and the condensation of neurofibrillae (*N F*) and tigroid substance. *B*, a fibrous astrocyte in an area of gliosis surrounding a tumor. *C*, an astroblast in an oligodendroglioma. *O*, oligodendroglia. Note the bifurcated process attached to blood vessel (*V*). The tissue is from a case brought to autopsy, and was fixed and preserved in a solution of formaldehyde for several years.

15. Clear in phenol-xylene-creosote [6] and mount in neutral xylene damar.[7]

Precautions.—Use reagent grade chemicals throughout. A glass rod, ¼ inch (0.64 cm.) thick, bent in the form of a hockey-stick (but not tapered), or for the larger sections a metal spatula drilled for a sieve effect and coated with paraffin, is suggested. Wash the transfer rod or spatula in distilled water before

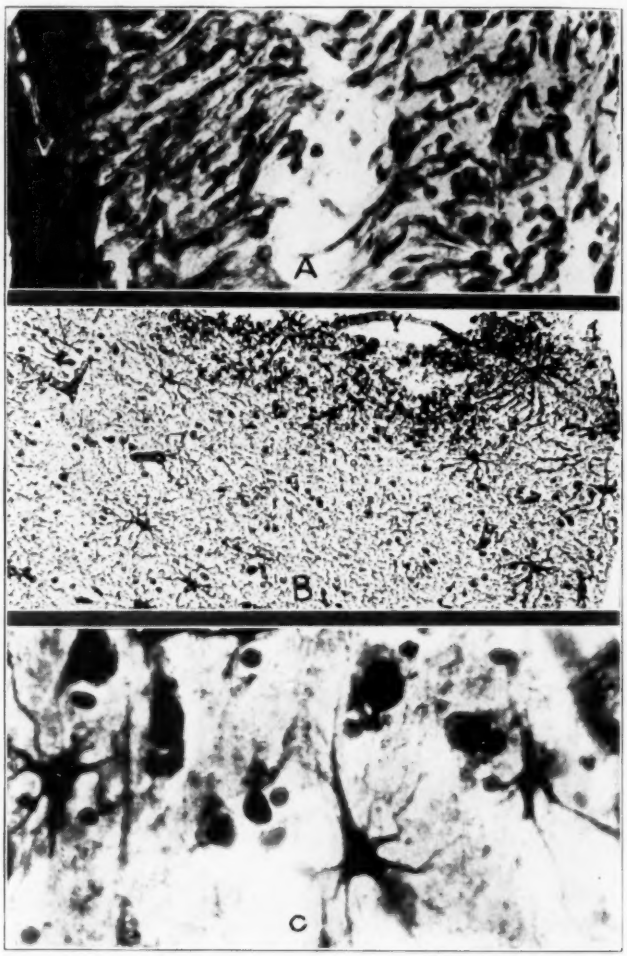

Fig. 3.—*A*, an average area from a spongioblastoma polare. With a hand lens both unipolar and bipolar types are seen. *B*, a field from a protoplasmic astrocytoma. Note the sucker process to the blood vessel (*V*) at the upper right. *C*, three fibrous astrocytes. Note the vascular sucker process.

6. The formula for phenol-xylene-creosote is: phenol, 1 part; beechwood creosote, 1 part, and xylene, 8 parts.

7. The formula for xylene damar is: saturated solution of gum damar in xylene, made neutral with calcium carbonate.

transferring from one solution to another, e. g., from silver to gold sublimate or from formaldehyde to the silver solution. All glassware should be cleaned in a sulphuric bichromate mixture, thoroughly washed, stored until use in a 5 per cent solution of nitric acid and when used washed thoroughly with tap water and several changes of distilled water.

Comment.—The method at first glance appears lengthy, but can easily be fitted to the time needs of the technician owing to the lack of rigid time require-

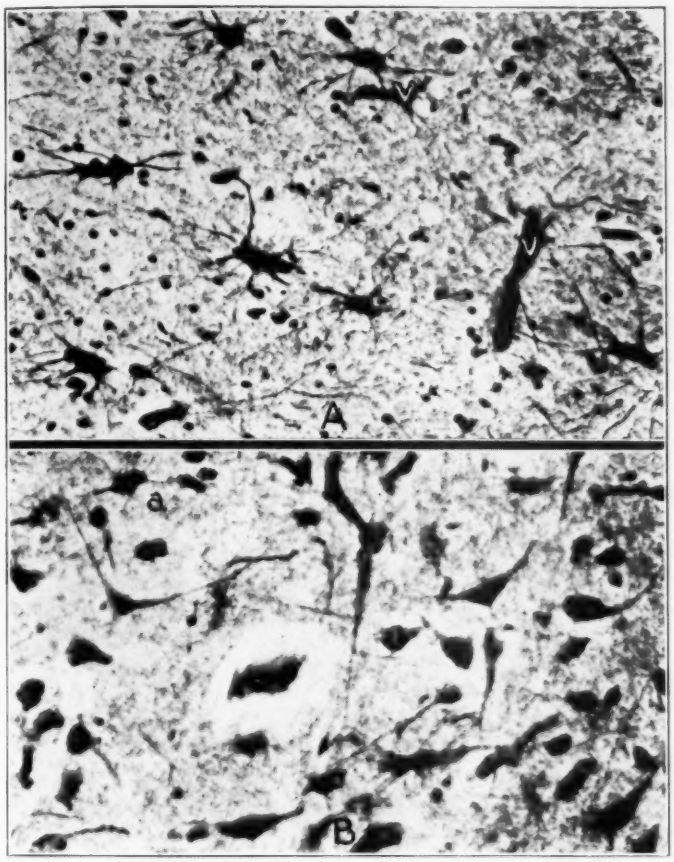

Fig. 4.—*A*, an area of gliosis surrounding a glioblastoma multiforme. *B*, glioblasts from an area of a glioblastoma multiforme; *a*, a fibrous astrocyte. The tissue, taken at autopsy, was fixed and preserved in solution of formaldehyde for several years.

ments. The bromine water has been found to be a most suitable mordant. The gold sublimate stains the tissue but lightly, the cellular elements appearing yellow or light brown, and the section grossly appears white or pale yellow. The gold sublimate acts, too, as a mordant for the silver. Toning in gold made alkaline either with lithium carbonate or sodium carbonate gives a grayish-white background, affording a better contrast for the cells, than with an acidified gold bath.

RESULTS

Ganglion Cells (figs. 1 and 2A).—The cells and the pathologic changes in them are well demonstrated. The perikaryon, with the Nissl substance, the axon and dendrites are brought out with remarkable clarity. The nucleus, its nucleolus and chromatin and any abnormal changes are easily recognized.

Axis-cylinders, of both medullated and nonmedullated types, are clearly brought out. They may be followed for great distances, the value of which is seen in studying degenerative phenomena.

Glia Cells.—Both adult and embryonic forms are stained.

Macroglia (figs. *2B, 3B, 3C,* 4*A*): Both the fibrillary and the protoplasmic types may be demonstrated. Unlike the usual preparations, they are not solid masses of black or purple, but a definite darker staining nucleus may be seen surrounded by a lighter perikaryon. The processes may be traced through many fields, some to distant blood vessels. These fibers appear to comprise a large part of the reticular substance. Any disturbance in the cells may be easily recognized.

Microglia and Oligodendroglia (fig. *2C*): These are likewise well shown. However, since the other cellular elements are well stained they are not as sharply contrasted by this method as they are in Hortega and Penfield [8] preparations. Gitter cells are clearly demonstrated.

Spongioblasts (Glioblasts) (figs. *3A,* 4*B*): Unlike the results in the usual gold and silver preparations, these cells are well stained.[9] They are clearly demonstrated, together with their processes, and the nucleus with its chromatin is sharply differentiated.

Astroblasts (fig. *2C*): These cells present the picture usually obtained with gold sublimate used with fresh tissues fixed with formaldehyde-bromide mixture.

SUMMARY

A staining procedure, utilizing both gold and silver, is offered as a simple routine method for demonstrating the neurons and glia of the nervous system. The preparations, not only with fairly fresh tissues but also with old tissues, are particularly suitable for photomicrography.

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8. Penfield, W.: Am. J. Path. **45**:178, 1927.

9. Bailey, Percival, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3.

A POSSIBLE EXPLANATION OF THE DWARFISM OCCURRING IN CERTAIN CASES OF HEREDOFAMILIAL DISEASE OF THE CENTRAL NERVOUS SYSTEM

FREDERICK LEMERE, M.D., DENVER

Mittelmann [1] recently reported four cases of dwarfism and ocular defects associated with heredofamilial disease of the central nervous system. These cases occurred in two generations of a Greek-Jewish family. The neurologic findings suggested disseminated involvement of the central nervous system with resulting incoordination, nystagmus, intention tremor and scanning speech.

The two cases to be presented in this paper were in patients of Mexican extraction. One was a girl, aged 13, and the other a boy, aged 6. Both showed advanced neurologic symptoms, dwarfism and ocular defects. A complete history, extending back over several generations, and examination of the immediate family failed to reveal any tendency toward similar degenerative changes in the parents, siblings or relatives. For this reason, a hereditary background such as Mittelmann described could not be demonstrated. Neither was there any history of consanguinity of the parents, as in Mittelmann's two most advanced cases.

REPORT OF CASES

CASE 1.—*History.*—Josephine Y., aged 13 (fig. 1), was the seventh of sixteen children. Her birth was normal, and she was breast fed to the age of 6 months. She walked at 1 year and talked at 1½ years. She had not had any serious illness, not even the usual diseases of childhood. Growth was slow, but not noticeably slow, till the age of 4 years.

At 4 years the patient began to walk with a wide base and often fell over, apparently from a lack of balance. Since then the patient has gradually regressed until now she is unable to stand alone unless supported by some one. Her speech has also regressed to a point at which she is unable to speak as well as she did at the age of 4. Her vocabulary is limited to a few words. She is unable to feed, dress or take care of herself and is incontinent at times.

Physical Examination.—The patient is small for her age but symmetrically proportioned. Her weight at the time of examination was 44 pounds (20 Kg.), the normal weight being 91 pounds (41.3 Kg.), and her height was 42 inches (106.6 cm.), the normal height being 58 4/5 inches (147.3 cm.). There was no evidence of the development of secondary sex characteristics. The muscles of the extremities were atrophied, apparently on the basis of disuse.

Neurologic examination showed marked generalized incoordination and inability to walk unassisted. There was intention tremor. Speech was in Mexican and

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This work was done on a Commonwealth Fellowship at the Colorado Psychopathic Hospital.

1. Mittelmann, Bela: Dwarfism and Ocular Defects in Heredofamilial Disease of the Central Nervous System, Arch. Neurol. & Psychiat. **30**:621 (Sept.) 1933.

Fig. 1 (case 1).—Appearance of the patient.

Fig. 2 (case 1).—Roentgenogram of the skull.

could not be tested. The reflexes were all hyperactive, except the abdominal ones, which were sluggish, especially on the right. There was a Hoffmann sign on each side, and a Babinski sign was elicited on the right. There was no spasticity of any muscles.

Ophthalmologic Examination: Nystagmus was present on looking in all directions. Skiascopy performed under mydriasis with atropine revealed hyperopia with high hyperopic astigmatism, indicating a rather advanced optic degeneration. The correction for the right eye was plus 1.50 sphere ⌒ plus 4.00 cylinder, axis 85; for the left eye, plus 1.75 sphere ⌒ plus 4.50 cylinder, axis 90.

Laboratory Findings: The results of the urinalysis and blood counts were within normal limits except for a low grade anemia. The Wassermann and Eagle tests of the blood were negative. Roentgenograms showed no evidence of achondroplasia or other bony deformity. The sella turcica was 20 per cent smaller than normal (fig. 2). The Wassermann and Eagle tests of the blood of both parents were negative.

Psychologic Examination: No definite measurement of the patient's intelligence was possible because of her inability to cooperate in the examination. Observation in the ward, however, suggested that it could not be classified higher than an idiot grade.

CASE 2.—*History.*—Paul V., aged 6 years (fig. 3), a brother of the first patient, was the tenth of sixteen children. His birth was normal, and he was breast fed till 5 months. He had pneumonia at 3 years and again at 5 years, with no other serious illnesses. He walked at 1½ years and talked at 2 years. Growth was slow, especially after the age of 5. At the age of 5 the patient started to walk with a wide base. Since then he has almost ceased to grow and has lost the ability to learn new words. Because of increasing ataxia, he has had to be fed and has difficulty in dressing himself.

Physical Examination.—The patient was stunted in growth but symmetrically proportioned. His weight at the time of examination was 32 pounds (14.5 Kg.), normal weight being 45 pounds (20.4 Kg.), and his height was 34 inches (86.4 cm.), the normal height being 43½ inches (110.5 cm.). Muscular development was fair, and nutrition was good. There was a suggestion of athetoid movements of the head and extremities.

Neurologic examination showed generalized incoordination, with ataxia and intention tremor. There was no spasticity. The patient could walk unassisted, but with a wide base. Speech could not be tested. The reflexes were hyperactive, but there were no pathologic reflexes.

Ophthalmologic Examination: Nystagmus was present on looking in all directions. Skiascopy performed under mydriasis with atropine showed marked hyperopia with hyperopic astigmatism. The correction for the right eye was plus 3.00 sphere ⌒ plus 2.50 cylinder, axis 115; for the left eye, plus 3.50 sphere ⌒ plus 2.25 cylinder, axis 50.

Laboratory Findings: The urinalysis and blood counts gave negative results except for a moderate degree of anemia. The Wassermann and Eagle tests of the blood were negative. Roentgenograms showed normal structure except for a skeletal development more consistent with the age of 4 than with the age of 6. There was no evidence of achondroplasia. The pituitary fossa was relatively smaller than normal (fig. 4). The Wassermann and Eagle tests of the blood of the parents were negative.

Psychologic Examination: A technical measurement of the patient's intelligence was impossible. Observation of the patient in the ward suggested that he belonged in the moron group.

Fig. 3 (case 2).—Appearance of the patient.

Fig. 4 (case 2).—Roentgenogram of the skull.

FAMILY BACKGROUND

The father of the two patients described was 52. He had always been healthy and was of average height and build. The mother was 46 and had always been well except for cholecystitis. Cholecystectomy, four years before the birth of the elder patient, entirely relieved her from symptoms and she had been well since. She was obese but not stunted in growth. During each of the sixteen pregnancies the mother had had hyperemesis gravidarum for two or three months before delivery. Five of the sixteen children had died, but the rest, excluding the two patients whose cases are described, were well and normal in stature and in intelligence. The five children who died were boys and were interspaced between the other children in regard to order of birth. The cause of death of three was not known; one died at birth, another at 5 months, and the third at 1 year. The fourth child died seven days after birth because of hemorrhage from the cord; the fifth died at 15 years from "nose bleed." There was no evidence of neurologic or ocular defects in any of the immediate family. There was no history of malnutrition or other injurious environmental factors.

COMMENT

No attempt will be made to discuss the differential diagnosis or review the literature on this particular neurologic and somatic syndrome. This has already been done adequately by Mittelmann.

The main concern of this paper is to report two additional cases and to suggest that the dwarfism is on a pituitary basis. In both cases reported here and in one of Mittelmann's cases the sella turcica was considered to be from 15 to 20 per cent under size.

The ocular defects were also of a degenerative nature and were more marked in the more advanced case. Both pituitary and ocular deficiencies might be expected in association with advanced neurologic degeneration. The endocrine system and sensory organs are certainly closely akin to the nervous system. Perhaps other glandular and sensory changes could have been found had it been possible to examine the patients in a more detailed manner.

SUMMARY AND CONCLUSIONS

Two cases of familial disease of the central nervous system in association with dwarfism and ocular defects have been described. The neurologic symptoms indicated a disseminated involvement of the central nervous system. The ocular defects were hyperopia and hyperopic astigmatism.

These two cases increase the total number of such cases reported in the literature to six, Mittelmann's four cases being the first to be described.

The patients reported on in this paper differ from those of Mittelmann in that they were of Mexican rather than Greek-Jewish parentage and there was no history of consanguinity or a hereditary background.

The dwarfism was probably based on pituitary underdevelopment, which could be demonstrated in both cases. The ocular changes were also probably on the basis of a primary degenerative process.

Because of the close relationship of the endocrine system and the sensory organs to the central nervous system, one might expect marked degenerative changes in the latter to be accompanied by similar changes in the former.

INCONTINENCE IN FAMILIAL SPASTIC PARALYSIS

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Familial spastic paralysis, or Strümpell's disease, is a rare heredodegenerative progressive disorder involving mainly the pyramidal tracts in the spinal cord. It is characterized clinically by weakness and rigidity of the lower limbs, with hyperactive and pathologic reflexes. However, as Paskind and Stone [1] said: "In a disease of this nature, however, it is hardly to be expected that the lesions should be confined exclusively to the pyramidal tracts; other parts may be and often are involved. . . ." These authors have added reports of cases in forty families, collected from the literature, to the one hundred and eleven family histories gathered by Rhein.[2] Jackson,[3] in addition to describing a family in which four cases occurred, brought the bibliography up to 1934. In all these studies many types other than the pure familial spastic paralysis have been recorded.

Thus, symptoms implying a circumscribed lateral sclerosis of the cord, a true Strümpell syndrome, have been found in only a relatively small number of cases. The various forms which the disease may take include, among others, spastic paralysis with involvement of the arms, with tremors, with cerebral or bulbar symptoms, with convulsions and with manifestations of multiple sclerosis. The difficulty, as with many diffuse degenerative diseases of the nervous system, is largely nosologic, and the subdivision into seven groups made by Rhein represents only a rough attempt at coordinating the disease pictures under one head. It seems better to think in the terms of Spiller,[4] who said that when other symptoms are found the condition may not be pure spastic paraplegia but is still a manifestation of an abiotrophy.

The standard definitions of familial spastic paralysis include the statement that usually no sensory or visceral changes take place. The occurrence of urinary and fetal incontinence in several members of a family suffering from this ailment (described in the following report) has led to a search for other cases of familial spastic paralysis with sphincteric difficulties reported in the literature.

REPORT OF CASES

The available information indicated abnormalities in four sisters and in their maternal grandfather. The grandfather was reputed to have had paralysis of the lower extremities at about the age of 40. The parents of the patients, three brothers, aged 25, 23 and 15, and two sisters, aged 14 and 8, were all normal. The parents were not relatives, and there was no evidence of syphilis in the family.

L. C., the oldest of the patients, developed normally until she reached the age of 23. She then noticed weakness of the right ankle, which would turn readily

1. Paskind, H. A., and Stone, T. T.: Familial Spastic Paralysis: Report of Three Cases in One Family and Observation at Necropsy, Arch. Neurol. & Psychiat. **30**:481 (Sept.) 1933.

2. Rhein, J. H. W.: J. Nerv. & Ment. Dis. **44**:115 and 224, 1916.

3. Jackson, A. H.: Familial Spastic Paralysis, Arch. Neurol. & Psychiat. **31**:1266 (June) 1934.

4. Spiller, W. G., in Osler, W.: Modern Medicine, Its Theory and Practice, Philadelphia, Lea & Febiger, 1910, vol. 7, p. 106.

and cause a tendency to fall. Within a year, gradual paralysis of the right lower extremity became manifest. At 24 there was urinary and fecal incontinence. Examination at 27 revealed complete spastic paralysis of the right lower, partial spastic paralysis of the left lower, and slight weakness of the right upper, extremity. The deep reflexes in the upper and lower extremities were hyperactive, and there was a pronounced bilateral Babinski sign. There was slight incoordination of both upper extremities. There was paresthesia of the right lower extremity, described by the patient "as if it were falling asleep." In addition, this extremity showed a diminished sensibility to touch and vibration. The last dorsal vertebra was prominent, but a roentgen examination of the spinal column gave negative results. There was no sphincteric sensation during involuntary defecation or urination.

M. C.'s right arm had not functioned well since infancy. She had been operated on for cervical spina bifida at the age of 4 years. At 6, the arms and legs became somewhat spastic. Examination at 11 showed weakness of the right hand and arm, with ataxia and inability to use the fingers for fine manipulations. The deep reflexes of the upper extremities were slightly overactive; those of the lower extremities were markedly overactive. There was bilateral patellar clonus, which was greater on the right side. Vibratory sensation was diminished bilaterally from the hips downward. There were no abnormal visceral manifestations.

E. C., aged 19, showed incomplete spina bifida of the lumbar and sacral regions; there were: talipes equinovarus, trophic ulcers of the feet and urinary incontinence about once a day.

H. C., aged 18, had pains only around the waistline and urinary incontinence of several months' duration.

COMMENT

Tooth [5] mentioned the occurrence of familial spastic paralysis and incontinence in three brothers. One of the patients, aged 29, "has lately had a tendency to commence passing his water before he is ready." Another, aged 12, "has a slight weakness of the sphincters, that is, he often fails to maintain control over the sphincter ani." The third, aged 13, "had the same bladder and rectum trouble that his brother has." Tooth added: "The weakness of the sphincters shown by some of them seems too slight in proportion to the other symptoms to possess any real diagnostic significance."

Newmark,[6] commenting on the cases of Tooth, said: "Despite the weakness of the sphincters and the anomaly of speech, Tooth assumes that primary lateral sclerosis is the anatomical basis of the affection, inferring this from the analogy of degeneration of the posterior tracts as the basis of Friedreich's hereditary ataxia. In regard to the disturbance of the sphincters and the difficulty of speech, Tooth's case resembles one of Latimer's, while the objections to the theory of pure lateral sclerosis do not exist in our cases."

Latimer [7] referred to a patient, aged 20, who occasionally had involuntary discharge of urine and feces, and to another, aged 18, who until the age of 10 years had involuntary micturition by day only. Rhein [2] reported the case of a patient, aged 8, in whom rectal control was lost. Other cases, abstracted from Rhein's review of the literature, are: Cafiero's [8] patient, aged 3, had sphincteric trouble;

5. Tooth, H. H.: St. Barth. Hosp. Rep. **27**:7, 1891.
6. Newmark, L.: Am. J. M. Sc. **105**:432, 1893.
7. Latimer, T. L.: Arch. Pediat. **7**:89, 1890.
8. Cafiero, C.: N. riv. clin.-terap. **14**:499, 1914.

Schönfeldt's,[9] aged 18, had a vesical disturbance; Lorrain's,[10] aged 36, had urinary incontinence; Kollarits',[11] age not given, had a sphincteric disturbance; Giovanardi's [12] patients, three brothers, aged 71, 70 and 69, had vesical disorders. Paskind and Stone [1] reported three cases, all in idiots, aged 11, 9 and 8, with incontinence of urine and feces. They also referred to two cases of Specht [13] in which there was a disturbance of the bladder.

SUMMARY

The case of a family presenting a condition for which the diagnosis of familial spastic paralysis, impure type, seems tenable is reported.

One member of this family had urinary and fecal incontinence; two others had urinary incontinence only.

Spina bifida was present in two of the patients. This is a rare occurrence in conjunction with familial spastic paralysis. No cases have been noted in the literature with this finding. Donini,[14] referred to by Paskind and Stone,[1] reported a case in which complete sacralization of the fifth lumbar vertebra was noted.

One case of familial spastic paralysis with talipes is reported. This finding has been noted occasionally.[1]

Sensory changes were noted in three of the cases.

Nineteen cases of familial spastic paralysis with sphincteric difficulties have been reported in the literature.

CONCLUSION

Visceral and sensory disturbances may be found in association with familial spastic paralysis.

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9. Schönfeldt: St. Petersburg med. Wchnschr. **23**:355, 1906.
10. Lorrain: Thèse de Paris, 1898.
11. Kollarits: Deutsche Ztschr. f. Nervenh. **30**:293, 1906.
12. Giovanardi: Riforma med. **12**:754, 1897.
13. Specht, R.: Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:176, 1924.
14. Donini, G.: Gior. di clin. med. **1**:401, 1920.

SPECIAL ARTICLES

SIR VICTOR HORSLEY
1857-1917

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Lineage, intelligence and the ability to work are a triad of attributes with which a single person is seldom endowed. Sir Victor Horsley was one thus favored. From his father's side came the blood of musicians and artists, and from his mother's side, not only that of artists but of surgeons as well.

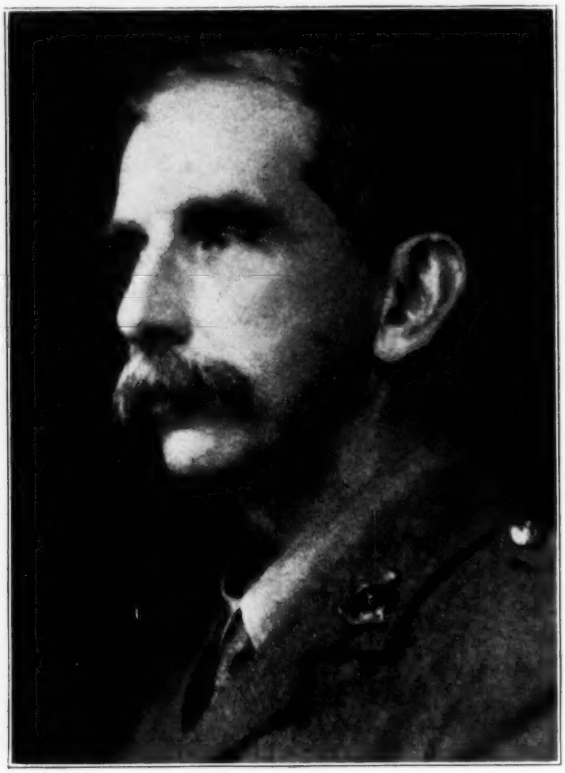
Born on April 14, 1857, he was named after the reigning queen, for she had taken notice of the fact that his birthday corresponded with that of the new princess, Beatrice.

His early years were those of a normal English schoolboy. He was not an exceptional student; he had an interest in many outdoor activities, and his sister remarked of him that he was "in almost perennial hot water." In 1873, at the age of 16, he began to show some evidence of scientific interest and was introduced by a friend to the use of a microscope. It was apparently at about this time that he became interested in medicine. In the same year he matriculated at the University of London. The next years were filled with efforts giving good promise of leadership: original work with the microscope, productive study and the recognition of his worth by his fellow students, as evidenced by his election to lead them. His energies were devoted unstintingly to doing each day's work well, and there are probably few lives that give better testimony to the worth of Carlyle's advice.

In 1878 he passed his examination for fellowship in the Royal College of Surgeons and also passed his first examination for the degree of Bachelor of Medicine, with distinct success. Thereafter he began his clinical associations, serving as clerk and dresser in the wards. In the next few years he had close association with Dr. Charlton Bastian, and in 1880 they published jointly in *Brain* what was the first printed writing bearing Horsley's name, entitled "The Arrest of Development in the Left Upper Limb, in Association with an Extremely Small Right Ascending Parietal Convolution." Likewise he had contact in this period with Gowers, another of the outstanding contributors to modern neurologic knowledge. This same year he qualified to practice, began his hospital service and necessarily broke the family ties which had contributed much to his development. This transition occurred at the age of 23.

Horsley had early in life become interested in the temperance movement and in the crusade against the use of tobacco. He had often

expressed his views in gatherings of friends. It was at about this transition stage that he made his first public sally in a semimoral field in a paper for the Students' Medical Society, "On the Evil Effects of Tobacco." Horsley was in no sense tolerant of individual selfishness when it impinged on what he considered the common weal. The most striking evidence of this is his lifelong attitude not only toward the abuse but toward the use of alcohol. This attitude became more and



SIR VICTOR HORSLEY
1857-1917

more fixed in the following years, so much so as to alienate many from his friendship. Of this trait his sister said:

> When Victor was a small boy, I think he was singularly easy going and good-tempered, showing none of that pugnacity, and impatience of other peoples' opinion, which marked his later life. . . .

In 1882 he was made surgical registrar of University College Hospital and was appointed assistant professor of pathology at University College. In 1884 he began a most profitable association with Professor

Schäfer, another with Charles Beevor and a third with an institution which must have come to represent to him a personality—the Brown Institution, which afforded him over a period of six years splendid opportunities in the newly opened field of physiologic research. Here he served as professor-superintendent, as did in their turn Burdon Sanderson, Sherrington and others of his peers. Here he carried on three major investigations: (1) studies in the localization of function in the brain and in the pathology of epilepsy, (2) studies on the thyroid gland, and (3) research on the preventive treatment of rabies. The last two investigations were outstanding pieces of work, but not, in Osler's opinion, of the same class with his many contributions to the surgery of the nervous system. In this view one must concur today. He had an amazing grasp of fundamentals and an ability to marshal them, two qualities which evidence themselves everywhere in his investigative work.

Because of his early association with neurologists and because of his appreciation of the opportunities offered by research in that field, it is not surprising that he concerned himself with the physiology and surgery of the nervous system. At each new step in his chosen field he made fundamental contributions. His birth was at a happy hour. Stimulated by the recently published work of Fritsch and Hitzig, and by that of David Ferrier particularly, he carried on research with E. A. Schäfer, with Beevor, with Spencer, with Semon and with Gotch, which covered the whole gamut of cerebral localization.

It was with such a background that Horsley approached his surgical work. In 1886 he was appointed surgeon to the National Hospital for the Paralyzed and Epileptic, Queen Square. Utilizing to the full the Listerian principles, which happily were now being recognized, and developing a technic which emphasized gentleness in the handling of tissues, he soon established the surgery of the nervous system on a secure basis only dreamed of by Godlee and MacEwen. By the end of the year Horsley had performed ten operations, with one death in the case of a boy long ill with a cerebellar tumor. Nor was he idle in the laboratory. There he was making experimental sallies in the field of surgery of the pituitary gland. At this time he was not yet 30 years of age.

The next year is memorable, for he performed the first successful operation for relief from a tumor of the spinal cord. Osler said of this event:

> In 1887 he removed successfully a tumor of the spinal cord, perhaps the most brilliant operation in the whole history of surgery. The victory was won. The young physiologist, trained in surgery by operating upon monkeys, had done what had hardly been dreamed of a generation earlier.

The year 1887 was of particular import to Horsley for another reason, for in this year he was married to Miss Eldred Bromwell to

whom he had been engaged for four years and whom he had known for many year before. Theirs was a community of ideals and of interests, giving impetus to the best efforts of each.

It is to Stephen Paget that one is indebted for a full biography of Horsley. As he pointed out, it is not difficult to trace Sir Victor's life to this point, but from there on it began to flow in various channels. Always there was the same incessant, restless pursuit, not of the chimera of success—for success came without effort—but of the satisfaction of work well done. Professionally, his advance was rapid. From 1891 to 1893 he served as Fullerian professor at the Royal Institute. In the latter year he was appointed full surgeon at the University College Hospital and also professor of pathology at University College, from which post he resigned in 1896 because of the increasing demands of his practice. In the following year he resigned as surgeon at the University College Hospital and was appointed consultant surgeon. Despite his rapidly increasing practice, he set time aside regularly for research, and this time was held well nigh inviolate. His keen interest in the investigative work of his many associates is amply witnessed on every side. He was never too busy to be of assistance to younger men. Frequently generous contributions of his own private funds made the pursuit of a problem possible. Through this period he served as one of the greatest champions of the cause of vivisection, and his help was of inestimable value, for not only did he fight for the cause but his work, in rabies particularly, was a splendid testimonial to the value of animal experimentation not only to man but to beast. If for that reason alone, British physiology owes him a great debt.

It was in this same period that he became an active worker in many social problems: the reorganization and revivification of the British Medical Association, the ardent support of temperance and the advance of woman's suffrage. All of these interests made heavy demands on his time, but his spirit and will seemed indomitable, and he carried on the work of two men, apparently never neglecting necessary details. Nor did he slight the development of his cultural interests; for example, he always entertained a keen interest in archeology.

Perhaps it is hasty to pass over so quickly those years which were the fruition of his life. Rather than his success in practice, however, is one interested in the spiritual legacy which he left to his profession. Motivating his entire life seems to have been that indefatigable energy which drove him through every day with constant focus on doing the best of which he was capable.

To attempt an appraisal of Sir Victor's character is a privilege which exposes one to the twin dangers of emotionalism and of hero-worship. In many ways he represents the true ideal of knighthood—brave and generous, chivalrous and gentle, intelligent, he was well called to knight-

hood in the true Arthurian sense. To these qualifications he added other attributes necessary to the surgeon: manual dexterity and resourcefulness.

It was his privilege to establish surgery of the nervous system on a solid foundation which contributed to no little extent to its amazingly rapid advance in the past fifty years. The fundamental reasons for his technical success Paget believed were: (1) his determination to avoid infections; (2) his familiarity with the action of anesthetics on the brain; (3) the substitution of the curved incision for the old cruciate type and the utilization of secure closure of the wound; (4) the use of rapid and nontraumatic methods of opening the skull; (5) the shunning of the use of the cautery, and (6) the use of wax to control bleeding from the cut edges of bone. These methods he combined with his intimate knowledge of the anatomy and physiology of the brain and spinal cord.

He was keenly interested in the social aspects of medicine and in social problems in general. He was a moralist and a champion of what he considered to be the right. J. S. Risien Russell said of him:

> No seeking after self-aggrandisement induced him to throw all his energies into a discussion of this or that problem, one motive and one alone, actuated him in doing whatever he did—was it right or was it wrong? Having made up his mind on this point, he would leave nothing undone to vindicate the right and crush the wrong, without in the least taking into account what effect his action might have on his reputation and career.

In retrospect, this phase of Horsley's character is perhaps of greatest interest. Nowhere in the comments on his life does one find a suggestion that Horsley ever vacillated in his own mind over what was right and what was wrong. He apparently had the faculty of making his judgments without the hesitation that comes to be second nature in most men trained in the scientific method of trial and error.

It was a tragedy that he was permitted to sacrifice his life in the World War, happy as he was to do so for his country. After service in France, Egypt and India, he died at Amara, on the Tigris River, on July 16, 1917, of heat stroke, at the age of 60. Yet he himself would not have wished it otherwise, and his was the final happiness of being spared the decadence of old age. He must often have wished this final blessing.

JOHN HUGHLINGS JACKSON
1835-1911

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No history of neurology can fail to give Hughlings Jackson a place among the great. Why this should be so would be easy to explain had he unearthed a panacea or mined a single perfect gem. His gift, however, was a subtle one, for it guided thought into new channels, and even today the penetrating surmise of this clinical philosopher continues to provide the modern student of the nervous system with constructive hypothesis.

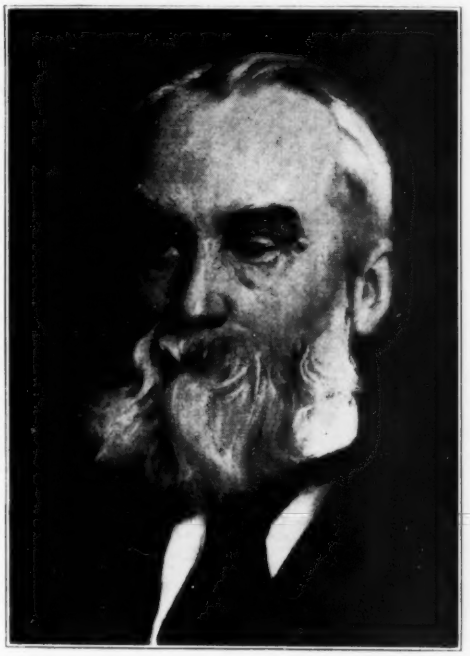
Never an experimentalist, he was satisfied with the belief that "there is no part of the nervous system that is not experimented on by disease." His raw material was a body of facts, facts that were gathered by himself or picked with care from the work of others. These he bound together and integrated into broad concepts which form a large part of present knowledge of the nervous system and its workings. Where they have failed as foundation stones they have proved serviceable scaffolding in their time. The medicine of today, so well equipped with the sick bed and the laboratory bench, might well reserve a place for the arm chair.

There is little in Jackson's early life to indicate the source of his gift for constructive thinking. He was born of rugged midland stock, the son of a Yorkshire farmer, his mother being of Welsh descent. Three brothers pioneered in New Zealand with distinction, but their attainments were not intellectual ones.

For Jackson there were the customary years of indifferent schooling, and an apprenticeship at York Medical School and St. Bartholomew's Hospital before he qualified as a physician in 1856 at the age of 20. Even the following three years of stimulating companionship with Dr. Laycock at the York Dispensary failed to shake his growing determination to quit medicine for the fields of philosophy. However, thanks to Jonathan Hutchinson he was persuaded to return to London, where hospital and teaching facilities were made available. Hutchinson never ceased to wonder whether he had done the world a good turn by taking Jackson's interest away from philosophy. There is no doubt in the minds of neurologists.

With encouragement from the brilliant Brown-Séquard, and doubtless because of the peculiar suitability of his mind, Jackson interested

himself in neurology. From that time until 1909 a continuous stream of important papers and observations came from his pen, based on his wide experience at Queen Square, at Moorfields Eye Hospital and in private practice. Moorfields Eye Hospital was the background for his wide knowledge of the ocular changes in nervous disease and his introduction of the ophthalmoscope to neurology. He never ceased to be grateful for this opportunity and spoke of it frequently during his life. His career in London became a busy round of hospital appointments, private practice and editorial duties. Through his collaboration with



JOHN HUGHLINGS JACKSON
1835-1911

Jonathan Hutchinson in the preparation of abstracts for various journals, he had opportunities to meet his colleagues, and he soon won their respect through his dignity, his speculative mind and his obvious intellectual attainments.

Jackson set to work on the huge material available to him in various London hospitals but was probably most active and most appreciated at Queen Square, where he gathered about him able and eager assistants. His house physicians remembered him with admiration and respect, although it is probable that they did not fully realize that his frequent and interesting speculations were really the enunciation of fundamental

principles. It is told that he did not spend a great deal of time in examining patients but was willing to spend hours discussing and speculating on the observations he had made. It goes without saying that his judgment and assessment of facts were extraordinarily near perfect. His relationship to patients was kindly and considerate, although detached. From his assistants he commanded interest and respect and sometimes deep affection. Of them he demanded accuracy and absolute honesty. He had no compromise to make with duplicity or slipshod thinking. He lost no opportunity to check his findings at autopsy and was humble when he was wrong.

Jackson's methods were simple enough, but they were applied with genius. They consisted of observation, the meticulous and unprejudiced observation of phenomena, the tabulation of facts in proper perspective, the harmonization of facts into a complete whole and finally generalization and the birth of a principle. Jackson was not a classifier of facts in the sense of the nosology of French neurologists, but rather a compounder of ideas and precepts. It is only necessary to glance through neurologic textbooks of the time to realize the confusion that existed through lack of determining principles. These principles were supplied by Jackson between 1861 and 1909 in a series of over 300 addresses, papers and discussions. They cover a field so enormous that no assessment can be attempted in a short biographic memoir. In various Hughlings Jackson lectures, Broadbent, Horsley, Head and others have dealt with special points. Jackson's writings include case reports, anatomicopathologic investigations, psychologic speculations and essays on physiologic mechanisms in the nervous system. They are a mine of clearly reasoned principles, philosophic and often ponderous, well documented, but always moderately stated and with the mark of intellectual honesty on them.

In early papers much consideration was given to the type of epileptiform seizures which now bears his name. Although Bravais in 1827 was the first to describe such convulsions of limited range and deliberate onset, Jackson further delineated the pattern and pointed out the common relationship to focal disease in the brain. Through postmortem studies he was led to the accurate localization of the lesions responsible and later to the much more important consideration of the mechanism involved in such attacks. His aim, however, was not merely to differentiate the epilepsy of coarse organic origin from the much more complex "idiopathic" type but rather to use the former as a foundation for the study of genuine epilepsy. "I trust I am studying the general subject of convulsions methodically when I work at the simplest varieties of occasional spasm I can find. We do not care to say that a tumour of the brain (or minute changes near it) had 'caused epilepsy', but that changes in a particular region of the nervous system 'led to con-

vulsions.'" Within a few years Jackson's epoch-making views on cortical localization won direct confirmation by the experiments of Fritsch and Hitzig in Germany and of Ferrier in Great Britain.

Largely on the basis of motor functions, Jackson viewed the central nervous system as divided into three levels, the lowest representing movements in their most simple form and made up of the medullary and spinal centers, the middle consisting of the motor cortex and the highest residing in the prefrontal area of rerepresentation. This division was based on the greater capacity for differentiation, specialization, integration and cooperation possessed by the higher levels as compared to the lower.

Corollary to this concept, Jackson developed the principle of "evolution" and "dissolution" in the nervous system. The more lately developed higher centers he looked on not only as more refined and complex, but also as possessed of inhibitory powers over the lower centers. Similarly, the highest centers, though formed last in the train of evolution, were first to suffer in the process of dissolution by decay from disease. Evolution implies not only a progressing increase of complexity and specialty but also that the higher (more complex and special) nervous arrangements control or inhibit the lower. There are two things: the "adding on" of the higher is at the same time a "keeping down" of the lower. Now as to the reverse process of dissolution; it also is a double process. The "taking off" of the higher is a "letting go" of the lower. On removal of the influence of some of the highest nervous arrangements (on loss of their function in cases of postepileptic mania by exhaustion), the next lower nervous arrangements, no longer controlled, spring into activity, and it is from their activity that the maniacal movements result.

In this light the positive symptoms of nervous disease are not the result of negative or destructive lesions, but rather the outcome of the action of normal structures released from the influence of the higher centers which have undergone decay through disease. In a series of papers and addresses Jackson illustrated the application of this principle in cases of hemiplegia, aphasia, postepileptic states and disorders of mentation.

Jackson's interest in disorders of speech has been admirably surveyed by Sir Henry Head in his Hughlings Jackson lectures. By careful clinical observation and the correlation of autopsy observations, Jackson was able to arrive independently at Broca's earlier localization of the speech center. Numerous other papers dealing with aphasia and related defects testify to the detailed accuracy of his approach to this subject. Vestibular vertigo, the ocular palsies and the function of the cerebellum were other fields which claimed his lifelong interest. Indeed, a study of his papers makes only too clear the impossibility of classifying his contributions or of listing his attainments. In their entirety they

represent an imponderable process of filtration to which the neurologic knowledge of the time was subjected. For the establishment of his views on evolution and dissolution in the nervous system, on disorders of the speech mechanism, on the doctrine of levels in the nervous system, on the mechanism and the differentiation of epilepsy and on other important subjects, Jackson had ideal mediums for the expression of his opinions. The journals were liberal with space; discussions were unhurried and developed on broad lines, and through his tenure of the Harveian, Lumleian, Hunterian and other honorary lectureships he was able to repeat and emphasize his principles. Despite this fact, one feels that Jackson's integrating principles have been woven into the fabric of neurology with less credit to him than his genius deserves.

Of the man himself, Jonathan Hutchinson (his closest friend), Taylor and others of his pupils have given interesting accounts. Dignified in appearance and serious in mien, he was a commanding figure in his wards or at any medical assembly. There was no all-embracing warmth about him, and his tremendous appeal to his students and assistants came from his character and intellect rather than from any broad humanity. He was fair-minded, scrupulously honest, never unjust and always the kindly gentleman. He could not have been overburdened with a sense of humor, although Taylor and others defend it. He had in its place the capacity for quiet amusement and the ability to see the inconsistency and absurdity in related happenings. Perhaps an unfair idea of his "heaviness" is given by his writings, which are complex, wordy and heavily documented. This was the result of his constant effort to avoid overstatement and to qualify his remarks. Excerpts from his conversation show that his tongue could be more pointed than his pen. Speaking of the auscultatory phenomena of heart disease, he has been quoted as saying: "Never treat a patient on stethescopic evidence only. The heart may be a bad musical instrument and yet a good force-pump." His love of plain speaking gave rise to many pointed rejoinders. A friend who had reviewed a certain author's book with such venom that he was threatened with personal violence complained to Jackson that he had done nothing to justify such anger. "That is very true," replied Jackson, "you did not shoot at the man; you shot only at his coat, but you must remember that it was on his back."

Jackson had no capacity to suffer boredom, and his patience lasted only as long as his interest. He would spend hours over the delineation of the pattern of a disease but would seldom sit to the end of a dinner. This curious eccentricity led him to attend the theater for but one act, to come to medical meetings only for the discussion or to break his frequent train journeys to his beloved Yorkshire as many as ten or twelve times before reaching his destination. His interests were not broad, and sport, music, art or the theater had little or no part in his

life. As a reader he was insatiable, and his tastes ran from philosophy to the worst penny dreadfuls. Of the philosophers, Herbert Spencer was his favorite, and of the novelists, he preferred Trollope, Jane Austen, Dickens and Thackeray. On his frequent excursions to Yorkshire his company was a penny thriller which he tore down the back and avidly read and forgot in sections. His great collection of books was largely emasculated by his curious habit of tearing out all the parts that interested him.

In 1865, Jackson married his talented cousin, Elizabeth Dade Jackson, who was his able and devoted companion until her death eleven years later. They were without children.

Jackson was a conservative in his leanings and has been likened to Samuel Johnson, whom he greatly admired. Certainly he had traditional views on the social and political questions of the time and shared Johnson's clarity of thought and force of assertion though he lacked his choleric temper. In the matter of religious faith he was the simplest kind of agnostic and would never assent to the formulation of any belief. He was a philosophic unbeliever and had no conception of a personal immortality after death. The conduct of his own life shows, however, that he governed it with his own high code of ethics.

Despite Jackson's great activity in London hospitals and his tirelessness in stating and restating his views, the full import of his observations gained recognition slowly. His addresses and papers were heavy, were couched in the philosophic language of Spencer and for the sake of accuracy were loaded with qualifications that took the edge off fundamental points. Many important contributions appeared in obscure journals and were not seen by continental workers. In his later years, however, he was able to see his concepts gradually incorporated in the body of neurologic knowledge, and he took great joy in the honors that came to him. The bestowal on him of numerous honorary lectureships, his election to fellowship in the Royal Society and degrees from Bologna, Leeds and other universities gave him great pleasure.

An interesting link with this country occurred in 1901 when Dr. Osler, on behalf of Dr. Weir Mitchell, Dr. James J. Putnam and himself, suggested to Dr. Jackson that he make an attempt to collect his papers for republication. This request brought a grateful reply from Jackson and stimulated him to make the attempt. Because of his failing health and the enormous burden of the work the desire was never realized, and he died of pneumonia in 1911 with the material scarcely touched.

Jackson's habit of thought is perhaps best reflected in his more abstract papers, of which his address on "The Psychology of Joking" is a good example. Here is a subject open to every able-bodied man with eyes and ears since the time of Adam. The master's analysis of

the commonplace was, however, a real contribution to psychology and to the discipline of thought.

Hughlings Jackson was no lone wolf in his elected field. He grew up with such brilliant workers as Bastian, Gowers, Ferrier, Gull and Ormerod but transcended them by his ability to etch the design of neurology into a harmonious and complete whole.

As with every great teacher, the written word and the spoken syllable formed but a small part of his great influence. A brilliant group of his inspired disciples have carried on under the stimulus not only of his teachings but of his method, his honesty and his lofty character. Henry Head, Gordon Holmes, James Collier, Edwin Bramwell, Kinnier Wilson, James Taylor and Risien Russell are but a few of those who have followed in the master's footsteps and through whom the master still speaks.

The key to the man's character has been aptly struck by one of his devoted pupils:

> Jackson's attitude was strictly phenomenal. He never deduced his observations from his hypothesis, but any hypothesis he enunciated sprang, as it were, ready made from some clinical fact. He stood like an observer on a bridge formulating the extent of the flood from matter carried down by the stream.

As Sir William Broadbent remarked:

> There are two kinds of knowledge, one consisting in the accumulation and verification of facts and their arrangement in their natural relation; the other of a more profound character, comprehending the underlying significance of phenomena. It is the last of these to which Hughlings Jackson has so largely contributed.

Jackson was not just an arm-chair philosopher. He was the general of a regiment of facts with a genius for marshaling and molding them into fundamental principles of science.

News and Comment

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

An examination of candidates for the certificate of the board in neurology, in psychiatry or in both neurology and psychiatry will be held at the Philadelphia General Hospital in Philadelphia on June 7 and 8, 1935, preceding the annual meeting of the American Medical Association in Atlantic City. It will include examination of patients, with reports on and discussions of findings, on June 7, and oral and written examinations in neuro-anatomy, neurophysiology, psychobiology, psychopathology, neuropathology and the interpretation of roentgenograms, on June 8.

Applications must be filed not later than April 8. Application blanks and further information can be secured from Dr. Walter Freeman, 1726 Eye Street N.W., Washington, D. C.

Abstracts from Current Literature

THE TREATMENT OF ACUTE HEAD INJURIES. GEOFFREY JEFFERSON, Brit. M. J. **2**:807 (Nov. 4) 1933.

Modern treatment of head injuries is chiefly nonoperative, because experience has shown that in the worst cases the patients are not saved by routine decompression. On the other hand, Jefferson thinks that the current fashion of administering hypertonic solutions in all cases of head injury is not advisable and that the practice needs revision.

The study here reported was an analysis of a consecutive series of 1,004 cases of head injury during a period of five years in one hospital and six years in another. Of the 1,004 patients, 23 per cent died. More important than the gross mortality rate is an analysis of the time of death; 60 per cent of the total eventual deaths occurred within twenty-four hours and the next highest number before the end of forty-eight hours. This primary mortality seems to be fixed and unavoidable, in the opinion of Jefferson, but the deaths which occur from the second or third day onward present an interesting problem. Some of them occur in aged people from pneumonia or exhaustion. Meningitis accounts for about 8 per cent. Subdural hematomas have been found more often in cases in which their presence was not suspected than in cases in which they were thought to be present. In addition, one can assume that damage occurs to the nerve centers and to the synaptic and tract connections following hemorrhage, secondary edema and necrosis, in which histamine may play a part. Many of these injuries might be recognized by proper clinical examinations.

Jefferson divides the patients into three major groups. The first group includes those who are deeply unconscious or comatose, with widely dilated pupils and sluggish corneal reflexes, cyanosis, stertorous respiration and flaccid limbs. These patients die soon and nothing can be done to save them. The second group consists of patients who are recovering consciousness when they reach the hospital; they have no recollection of the accident; they are in a state of shock, vomit once or several times and are dazed and restless, but can be induced to answer questions. Often these patients do not again lapse into unconsciousness, and though they may be drowsy and restless they can usually be roused periodically for a sufficiently thorough general and neurologic examination. It is important to recognize that fractures of the skull may be present in patients with this type of case and, what is more important, that there may be laceration of the brain. It is from this class that the best examples of extradural and subdural hematoma are recruited. Some of these patients again relapse into unconsciousness or into a stupor from which it is difficult to rouse them. Unless careful observations have been made on admission, they then present difficult problems. The crucial point is the depth of secondary unconsciousness and the presence or absence of localized signs. If the stupor is relatively light and no weakness of the limbs is present a clot can be assumed to be absent, but if there is the slightest doubt it is much wiser to explore operatively to establish the presence or absence of intracranial bleeding. The third group presents the greatest difficulty in diagnosis and treatment. These are patients who are admitted in a state of stupor or semistupor and who remain noncooperative and unresponsive for many hours or days. Their general condition may not be bad. They are well oxygenated; the pupils are normal. Although they are designated as unconscious, much information can be gathered if the observer will take the trouble to sit by them for a time. Facial asymmetry may be observed by testing the corneal reflexes; movements of the arms may be watched during efforts to remove an annoying finger from the cornea; the abdominal, plantar and tendon reflexes furnish corroborative evidence of a unilateral

lesion. Perfunctory examination of reflexes ought to be replaced by careful notes on movements of the limbs during the restless turning of these patients and a search made for evidences of damage to cerebral centers.

The cause of traumatic stupor is discussed, and Jefferson concludes that stupor in the average case is contusional; even when edema occurs, it is rarely alone the cause of protracted unconsciousness. He believes that it is most often due to contusion of the anterior portions of the hemispheres. Patients remaining unconscious for any length of time may safely be assumed to have suffered neural damage. Incontinence is particularly frequent in diseases of the frontal lobes, and sometimes of the temporal; it is rare with lesions in other areas. Incontinence is the rule in severe head injuries and is interpreted as a symptom of damage to the same area of the brain as when it occurs in tumors. Anosmia is another localizing sign of frontal contusion. Failure to recognize aphasia as an important localizing sign has cost more than one patient his life.

The use of hypertonic saline solutions is discussed. "I believe," says Jefferson, "that their use is incorrect if we expect them to return a patient to consciousness." The patient is not unconscious because his brain is edematous but because it has been damaged generally, and probably locally as well, by a severe blow. If the damage is not too severe, and if no new element is added, the patient will eventually recover no matter how he is treated. Subdural bleeding is an event for which one must be ever on the watch. Intravenously administered hypertonic saline solutions not only raise the blood pressure, but by shrinking the brain increase the space into which hemorrhage may occur. During the first day or so, hypertonic solutions are best withheld and should be used only when indicated by a manometric reading of the cerebrospinal fluid. This should not be done during the first twenty-four hours. Readings are valueless if the patient is restless. The only time when dehydration is of service is during secondary edema, and that means from the second or third day onward. Middle meningeal hemorrhage and subdural hemorrhage may cause confusion in diagnosis. A patient with a subdural hemorrhage may not be unconscious, though he will become so eventually if unrelieved. The pulse rate in cases of head injury is not in itself an indication for operation. A very slow pulse rate is a danger signal, but it can well be a false alarm. On the whole, low pulse rates are observed during the first few hours more commonly in fatal cases than in others. Secondary bradycardia, setting in toward the end of the first week and continuing into the second, is not uncommon from reactionary edema. In these cases, contrary to expectations, the cerebrospinal fluid pressure would not necessarily be elevated.

FERGUSON, Niagara Falls, N. Y.

THE DIAGNOSIS, TREATMENT AND IMMEDIATE PROGNOSIS OF CEREBRAL TRAUMA: AN INTRODUCTORY STUDY OF 1,494 CASES. DONALD MUNRO, New England J. Med. **210**:287 (Feb. 8) 1934.

Aroused by an editorial in the *New England Journal of Medicine* implying that the diagnosis and prognosis in cases of cerebral trauma are poorly understood and that the present-day methods of treatment are neither essential nor valuable, Munro presents the results of a study of 1,494 cases in an endeavor to refute these statements. In addition, he considers critically certain statements heretofore widely accepted relative to the physiopathologic characteristics of cerebral injuries.

The material is drawn from patients admitted to the Boston City Hospital over a period of four and one-half years; 505, or approximately one third of the group, were under Munro's personal observation in the neurosurgical service. This preliminary paper deals only with the common types of cerebral and skull injury, including simple linear fracture, concussion, congestion and edema and contusion and laceration of the brain. A method of treatment consisting of the proper care of surgical shock, when present, and therapeutic dehydration in association with decompression by repeated lumbar drainage is described. The importance of

modifying treatment in relation to the pathologic process actually present is emphasized; routine methods are condemned.

Lumbar puncture used as a decompressive agent is safe and effective; by appropriate comparisons of analogous groups of cases it is demonstrated that an increase in the number of patients treated primarily by lumbar puncture is associated with a corresponding decrease in the mortality of the group. The maximum allowable mortality is placed between 10 and 11 per cent, with a further statement that "a 20 per cent group mortality implies inaccurate diagnosis, improperly applied treatment or lack of experience with a sufficiently large number of cases." Failure on the part of the patient to improve under this system is further held by the author as sufficient warranty to justify bilateral temporal trephination, as an exploratory measure, to locate or to rule out an undiagnosable and untreated meningeal hemorrhage.

Under appropriate sections considerable space is given to a discussion of certain popular misconceptions having to do with the production of contrecoup injury, the mechanism of the arrest of intracranial hemorrhage and the so-called therapeutic use of morphine. The last two in particular deserve especial mention, because when improperly understood either may lead to unnecessary death or invalidism.

The statement by Russell in *Brain* that "increased intracranial pressure provides a powerful means of controlling hemorrhage from torn capillaries and veins" is characterized as a gross inaccuracy, even though a belief in this fallacy is widespread among the medical profession. Experimentally, it is known that increased intracranial pressure is associated with a slowing of the blood flow and dilatation of the veins and arteries; if severe, this stasis may produce anoxemia with cellular destruction, petechial softening, edema, further stasis and capillary hemorrhages throughout the brain. Such small areas of destruction coalesce with a further spread of the process and further destruction of tissue. Clinically, this progression is evident. It is obvious, therefore, that high intracranial pressure cannot cause hemostasis without also causing anoxemia and necrosis of the brain. By the same token, lowering a high intracranial pressure by lumbar puncture decreases venous bleeding, because the venous pressure falls with the lowering of the cerebrospinal fluid pressure. The venous pressure is high because the intracranial pressure is high.

The use of morphine in these cases is held to be a "most pernicious teaching and cannot be condemned too strongly." It is pointed out that the disease is one that of itself kills by paralyzing the respiratory centers, and the folly of adding the burden of a strong respiratory depressant to an already embarrassed center should be obvious. "No morphine where increased intracranial pressure is suspected" should be an axiom.

The paper is epitomized in nine conclusions, which are sufficiently categorical to be easily understood and which can be made to serve as a useful guide to the general surgeon or physician who sees these cases only once in a while.

Dr. Munro's conclusions follow:

"1. The diagnosis of craniocerebral injury is firmly established on a pathological basis. It includes linear, depressed and compound fractures; concussion, edema, contusion and laceration of the brain, extra- and subdural hemorrhage, and a few other less common forms of skull and brain injury.

"2. The immediate prognosis of cerebral injury after head trauma can be fairly good. In this series of 1,494 cases the mortality was 17 per cent. In a group of 405 cases of common types of brain and skull injury, the mortality was 10.3 per cent. A 20 per cent group mortality implies inaccurate diagnosis, improperly applied treatment or lack of experience with a sufficiently large number of cases.

"3. One treatment for the usual forms of brain injury has been standardized. It consists of the preliminary treatment of surgical shock, when present, followed by therapeutic dehydration and repeated lumbar puncture for decompression. Treatment of compound and depressed fractures, meningeal hemorrhage, and the less common forms of brain injury is not considered in this paper.

"4. If improvement does not set in and continue under this treatment, and if toxic dehydration and meningitis can be ruled out, bilateral exploratory temporal trephines are indicated to eliminate the possibility of undiagnosed sub- or extradural hemorrhage, or one of the less common types of brain injury.

"5. Cases treated as above, or by lumbar puncture alone, have a mortality 9 per cent less than similar cases treated without lumbar puncture.

"6. In over 1,000 lumbar punctures for decompression in acute brain injuries there has been no death attributable to this procedure.

"7. Therapeutic dehydration is suitable treatment for traumatic edema of the brain. In combination with decompression by lumbar puncture it is suitable treatment for traumatic contusion and laceration of the brain. Improperly used it may cause unexpected and severe symptoms.

"8. The use of morphine is dangerous in cases where increased intracranial pressure is suspected. It should never be administered under such circumstances.

"9. Increased intracranial pressure does not aid in the prevention of bleeding from the cerebral vessels."

COBB, Boston.

CEREBRAL INVOLVEMENT IN HEAD INJURY: A STUDY BASED ON THE EXAMINATION OF TWO HUNDRED CASES. W. RITCHIE RUSSELL, Brain **55**:549 (Dec.) 1932.

The incidence of injury of the head reaches its maximum between the ages of 20 and 30 years, and is accounted for chiefly by motorcycle accidents; the general incidence among males is much greater than that among females. After the age of 40, the percentage of fatal results rises greatly. From a study of the temperature, pulse and respiration in cases grouped according to duration of loss of consciousness, it appears that the condition of the pulse is an important prognostic guide. A tendency for the pulse to become progressively more rapid and feeble is a sign of grave prognostic significance. Among the cases studied increased intracranial pressure did not contribute to a fatal issue. Complete absence of headache in cases of both slight and severe injury was not uncommon. Vomiting seemed to have no significance. Evidence of damage of the fifth, ninth, tenth, eleventh or twelfth cranial nerves was detected in no case. One pyramidal tract had been more damaged than the other in 14 cases. Rigidity of the muscles of the neck was found to a slight degree in 38 cases and to a marked degree in 28. In 69 cases retrograde amnesia lasted for one or two seconds, in 24 cases for several minutes and in 3 cases for longer than half an hour. There was no relationship between the degree of unconsciousness and the pressure of the cerebrospinal fluid.

It is probable that the presence of severe headache indicates that the intracranial pressure is raised. The findings suggest that a large quantity of blood in the subarachnoid space may cause, of itself, loss of consciousness. It is suggested that the common contrecoup injury is caused by the brain tearing itself from its own coverings by the force of its own momentum. The ancient conception of a commotion occurring in the nerve elements is accepted as the explanation for the sudden loss of consciousness. The degree of injury to the skull and brain must depend (1) on the rapidity with which the momentum of the brain and skull is altered and (2) on the degree of change of momentum.

In 61 per cent of the 141 cases examined, symptoms which were presumably caused by the injury had been present since discharge. It is pointed out that detailed analysis of the subjective features of genuine postconcussional disturbances is important. Various views in regard to the pathologic process of concussion are discussed. The chief possible complications are: aspiration of blood and nasal secretions into the lungs, infection spreading to the meninges and brain, cerebral edema and intracranial hemorrhage. A rational basis of treatment is outlined.

MICHAELS, Boston.

AN UNUSUAL FORM OF CEREBELLAR HEREDO-ATAXIA. MAX BIELSCHOWSKY, L. BOUMAN and W. G. SILLEVIS SMITT, Jahrb. f. Psychiat. u. Neurol. **51**:1, 1934.

The authors report the case of a man, aged 55, who at 27 had begun to show slight clumsiness of motility and indistinctness of speech. He was able to continue his work until the age of 40, when there developed attacks of petit and grand mal with periods of confusion. Neurologic examination at this time showed incoordination of gait and station, a positive Bárány test and marked dysarthria. The patient remained in this condition until death in stupor during status epilepticus. The family history reveals the following facts: one brother suffered from a marked cerebellar syndrome and a "paranoid psychosis;" a sister had a cerebellar gait and was demented; the father, who was addicted to the use of alcohol, late in life experienced difficulty in walking and committed suicide by drowning; the paternal grandfather was also a heavy drinker and committed suicide by drowning. The patient had six healthy children; the youngest, a girl, aged 11 years, had depressed tendon reflexes, slight but definite nystagmus and slight ataxia of the upper and lower extremities.

Necropsy revealed that the vermis and cerebellar hemispheres were one third their usual size. The cerebellar convolutions were markedly narrowed, and the sulci were unusually deep, the entire organ being extremely hard. Histologic examination of the cerebellar cortex showed marked atrophy; the molecular layer was narrow and in striking contrast to the better preserved granular layer, although this layer, owing to the loss of many granules, also appeared pale. Between the molecular and the granular layer there was a sharply outlined cellular zone consisting of glial elements which actually represent the cells of origin of the Bergmann vertical fibers, which were considerably increased in number. The Purkinje cells had been almost totally destroyed; only here and there was there one of these cells, which appeared shrunken and had poorly developed, and in areas club-shaped, dendrites. The cerebellar nuclei showed slight alterations as evidenced by a slight diminution of myelin fibers and a corresponding increase of glia fibers. The olives, together with the dorsal and mesial accessory olives, were almost totally devoid of ganglion cells; the entire structure of these nuclei seemed to consist of a coarse glial network; corresponding to these changes the fibrae arcuatae and the olivary portions of the corpora restiformia were also unusually pale. The pontile fibers and ganglia showed no noteworthy alterations except that the dorsal portion of the pons gave the impression that the gray substance was not completely matured. In studying the relationship beween the nuclei and the bodies of the ganglion cells in this region the impression was gained that these were more or less embryonal in nature. The alterations in the spinal cord, though slight, were nevertheless definite and left no doubt that they were not accidental; the posterior columns showed degeneration, which could be followed through the entire length of the medulla spinalis and was limited to the region of the posterior longitudinal septum.

In addition to these typical pathologic changes of cerebellar ataxia, histologic examination also disclosed collections of corpora amylacea in the subependymal layers of all ventricles and in the subpial region over the cerebral convolutions; in the stratum zonale these bodies formed almost a continuous layer, consisting of several rows. Several glia cells also contained small grapelike collections of mucous globules; these seemed to have a great affinity for hematoxylin and the usual basic aniline dyes; they were found also in larger numbers in the adventitial sheaths of the larger blood vessels. Another unusual finding was two small tumors under the ependyma of the posterior portion of the fourth ventricle; they were symmetrically situated on the two sides between the dorsal vagus nucleus and the floor of the fourth ventricle. The histologic picture resembled that of the ganglioneuromas, so that the authors regard them as stigmas of the degenerative constitution. Still another unusual finding was the frequent occurrence of ganglion cells with typical Alzheimer fibrillary processes, especially in the frontal and temporal lobes of both hemispheres in which they were limited

exclusively to Brodmann's third layer (lamina pyramidalis). These peculiar ganglion cells, the authors believe, are the substratum for the abnormal psychic manifestations which the patient showed during life.

The sections also showed a more or less general increase in the glia, which was most marked in the frontal convolutions and in the deeper layers of the white substance of both hemispheres; in some areas these glia cells appeared in the form of nests and star-shaped formations. The ganglion cells in Sommer's sector, though not diminished in number, appeared shrunken and covered by proliferated oligodendroglia cells. Finally, numerous giant cells poor in chromatin were found especially in the striatum and pallidum, although here and there similar cells were observed also in other regions, including the cerebral cortex. The authors are at a loss to explain the significance of these cells as well as of the peculiar glial formations.

KESCHNER, New York.

POLIOMYELITIS. F. M. R. WALSHE, Brit. M. J. **2**:1197 (Dec. 30) 1933.

Walshe confines himself for the most part to a brief consideration of the question of specific treatment of poliomyelitis in the light of the rapidly changing conception of its nature. Poliomyelitis, epidemic encephalitis and rabies are infections of the nervous system due to ultramicroscopic viruses which attack essentially the gray matter and for this reason are spoken of as polioclastic. They multiply only in contact with the living cell, within which their life and activity appear to be very brief; because of this the conditions they produce may be spoken of as self-limiting diseases.

During the past four or five years a marked change has taken place in the concept of the pathologic process of poliomyelitis. Until then it was looked on as an acute specific fever with three distinct clinical and pathologic phases. Clinically, there were an initial, short-lived phase of systemic infection with constitutional disturbances, then signs and symptoms of meningeal irritation and finally involvement of the nerve tissue, namely, paralysis. The primary lesion of the nerves was believed to be meningitis which spread along blood vessels into the cord, affecting first the interstitial tissue and second the nerve cells. The port of entry of the virus was believed to be the nasopharynx, through the perineural lymphatics in the subarachnoid space. Pathologic investigation reveals that the virus reaches the nervous system by the axis-cylinders of the olfactory nerve, enters the olfactory bulbs and is spread thence within the nervous system by axonal channels. It has a special affinity for the nerve cells of the cervical and lumbar enlargements of the cord, within which it appears to multiply most easily. The primary lesion is of the nerve cell and not of the interstitial tissue. The cerebrospinal fluid has been found to play no essential part in the carriage of the virus, and the meningeal reaction has been found to be the result and not the precursor of the direct attack on the nerve cell by the virus. In the light of this known pathologic course, the clinical symptoms can be interpreted in a different manner than formerly; what was looked on as systemic infection is only the opening clinical phase of primary involvement of the nervous system. Trained observers soon appreciate the differences between the usual infections of childhood and those of poliomyelitis. There is a look of mingled apprehension and resentfulness, quite unlike the alert, bright and shining eyes seen in other types of fever. Further psychic change is revealed in the annoyed shrugging of the shoulders which occurs when the child is touched or spoken to. There is frequently even a snarling whine of resentment, which is synchronous with this gesture of discontent. When the infection is even more pronounced, the child is restless, breathes rapidly and seems to be busily and actively resisting some incomprehensible disturbance of its usual comfort. In these instances the irritability and resentful manner are not marked, but the whole organism seems to be composed of tensely drawn wires—a universal overstimulation. The pressor state of the nervous system is so marked that a sort of impulsive ataxic tremor is present in every motion, especially when that motion has intent. Thus the development of paralysis does

not, as has formerly been assumed, indicate the entry of the virus into the nerve cells or the onset of the attack on them. In other words, the attack on the nerve cells has begun before diagnosis is possible.

This new concept of the clinical course of the pathologic condition in poliomyelitis explains a great deal in regard to efforts to treat this condition, especially with serum. The preparalytic stage of poliomyelitis is that stage of the disease in which the nerve cells have not yet been destroyed or paralyzed. Walshe reviews the history of serum treatment for this disease and concludes that, with the exception of three series of cases, serum treatment in the past has not been conducted on a basis that makes an assessment of its value possible; when definite scientific controls were utilized, those who did not receive serum reacted just as well as those who did, and there is even some indication that they reacted better. In conclusion he says that it is well to look the situation in the face and realize that from the very nature of the disease one cannot be sanguine about any method of treatment that can have effect only after the nerve cells already harbor the virus and are suffering from its attack. He thinks that the production of an active immunity offers the best hope for the control of the disease.

FERGUSON, Niagara Falls, N. Y.

DIAGNOSIS AND TREATMENT OF FRACTURED SKULLS. L. T. WRIGHT, J. L. GREENE and D. H. SMITH, Arch. Surg. **27**:878 (Nov.) 1933.

The authors analyze 347 consecutive cases of cranial and intracranial injuries in which the patients were treated at the Harlem Hospital. An attempt was made during the progress of the study to include only (1) fractures of the skull proved by roentgen examination or autopsy (133 cases) and (2) intracranial injuries without fractured skull as demonstrated by a history of trauma and blood in the spinal fluid (85 cases). The mortality in the latter group is only about one third of that in cases of proved fracture of the skull.

The frequency of coexistent acute alcoholism (18.8 per cent), a percentage which is believed to be too low in this series, plays an important rôle in the diagnosis and progress in these cases. As is usual with recent reports, the automobile is the leading causative factor in the production of the injuries. Likewise, the better prognosis for life in cases of craniocerebral accidents in children is confirmed. Fifty-two per cent of the deaths occurred within the first twelve hours after admission, while those delayed more than forty-eight hours were largely due to complications, with the exception of extradural hemorrhage, rather than directly to the cerebral injury.

Strict definitions of the terms concussion, contusion and laceration of the brain are adopted. In cases of laceration, the spinal fluid is invariably bloody. Epidural hemorrhage, the cause of 10 per cent of the fatalities, is always associated with fracture of the skull which ruptures the middle meningeal artery or one of its branches, generally at the intersection of the vessel and the fracture line. The usually described lucid interval occurred in only a single case of this type.

The rôle of cerebral edema is believed to be greatly exaggerated in craniocerebral injuries. The occurrence of hypotension of the spinal fluid and of a shrunken or a nonswollen brain at operation is not uncommon. Hemorrhage explains the chief increase in intracranial tension, while the rôle that alcohol plays should be considered. Moreover, cerebral edema is often a late development. The poor prognosis in cases with unconsciousness, fixed and widely dilated pupils, bleeding from the ears, escape of cerebrospinal fluid, convulsions, urinary incontinence and glycosuria is confirmed. The prognostic value of changes in temperature, pulse and blood pressure demands interpretation in relation to the general symptomatic picture. Likewise, the value of readings of the spinal fluid pressure, which were made as a routine, merits careful evaluation. The erythrocyte and leukocyte counts of the spinal fluid bore a definite relation to the severity of the injury. Roentgenograms were obtained in 75 per cent of the cases.

Conservative nonoperative treatment is strongly advised. The intravenous injection of hypertonic solutions is not favored, in the belief that a secondary rise in intracranial pressure results. The use of lumbar drainage is likewise looked on with disfavor. The combination of lumbar drainage and limitation of fluid intake, tried in 15 cases, proved disappointing. Rest, sedation and maintenance of nutrition and warmth were chiefly relied on. Operation was performed 18 times as follows: in all cases of compound depressed fractures, in some cases of simple depressed fractures and in cases in which epidural hemorrhage was suspected.

SPERLING, Philadelphia.

THE SIGNIFICANCE OF THE AMERICAN DISTRIBUTION OF TABES AND PARESIS. WILLIAM F. PETERSEN, Am. J. Syph. & Neurol. **18**:75 (Jan.) 1934.

In spite of the high incidence of syphilis in the tropics, tabes and dementia paralytica are relatively rarer there than in temperate zones. Petersen believes that this can be accounted for largely on a meteorological basis. Significant and rapid changes in the barometric pressure will be reflected in the endocrine tide, activity of the bone marrow, blood chemistry and blood pressure. In the spring, the acidity of the organism is enhanced by repeated stimuli, while in the fall, as a result of meteorological stability, sunshine, vegetable diet and similar factors, the body is relatively alkaline. Within the United States are areas of great barometric instability, known as "storm tracks"; inhabitants of these regions undergo a constant rhythm of metabolic change from a state of vascular spasm, alkalinity and low oxidation to one of vascular dilatation, high oxidation and a preponderance of catabolic activity. During the latter phase, spirochetes are destroyed much more readily than during the anabolic stage. In the tropics, on the other hand, these rapid meteorological changes do not occur; there is seldom a period of vascular spasm and low oxidation. If spasm is injurious to the spirochete, it is more so to the tissue—especially that tissue supplied by terminal vessels. This type of vascularization is found especially in the central nervous system. On this theoretical basis, therefore, one might assume that disorders dependent on degeneration of nerve tissue would be more prevalent in the "storm track" regions of the United States than elsewhere.

Petersen demonstrates that this geographic correlation does exist, by presenting maps of the major storm tracks of the United States and also maps illustrating the incidence of tabes and dementia paralytica. The areas of meteorological instability are concentrated chiefly in the northern section of the country, notably in New England. The distribution of parenchymatous syphilis of the central nervous system shows a striking similarity to this arrangement. Further proof of the concordance of these phenomena is offered by an analysis of the distribution of general and vascular syphilis in the United States. A study of this incidence shows the highest rate of syphilis to be in the southeastern section of the country. It appears that a high rate of syphilitic infection without the added factor of meteorological disturbance is followed by a low incidence of tabes and dementia paralytica. Other factors which might bring about vascular spasm, such as ergotism, pellagra, pernicious anemia, plumbism and even emotional disturbances, will likewise be associated with a disproportionately high incidence of parenchymatous neurosyphilis.

DAVIDSON, Newark, N. J.

THE PSYCHO-ANALYSIS OF THE UNCANNY. EDMUND BERGLER, Internat. J. Psycho-Analysis **15**:215 (April-July) 1934.

In childhood there is a feeling of omnipotence which is suppressed in the development of the child. When, however, something happens and the repressed infantile feeling of omnipotence reveals itself, one gets a sensation of something taking place which is uncanny. The same thing takes place when repressed primitive beliefs prove really to be true. The feeling of the uncanny is really a saving

of anxiety, which will develop otherwise when infantile wishes come to the surface. Anything which exceeds the ordinary average is often called uncanny. For this reason many people avoid anything but the average all their lives. In the sense of the uncanny, one takes alarm at one's own omnipotence, which for a few seconds is imagined to exist. This is tied up with the child's oedipus situation and the fear of castration. The sense of the uncanny may appear when one watches another person showing aggressive tendencies, for example, when one hears a man coldly discussing the discharge of a large number of employees from his service who would obviously starve. A sense of the uncanny may develop when one sees somebody suddenly fall from his high position or suddenly lose his power. Manifestations of unconscious psychic forces arouse a sense of the uncanny; for example, a woman reveals that for many days she has had the uncanny feeling that she ought to tell her husband about her unfaithfulness, which is, of course, nothing other than a desire for punishment. Cynicism can often give the sense of the uncanny; for example, one has such a feeling when considering a man who is cynical at the hour of his death. An impenetrable silence on the part of another person gives also the same sensation, as is exemplified in the striking visit to Robespierre in Barras' "Memoirs." A sense of the uncanny may be experienced when that which was begun in play passes into deadly earnest. There is excellent literary material illustrating the various points, which Bergler covers in a scholarly, competent manner.

KASANIN, Howard, R. I.

CONSTITUTIONAL FACTORS IN HOMOSEXUALITY. GEORGE W. HENRY and HUGH GALBRAITH, Am. J. Psychiat. **13**:1249 (May) 1934.

Homosexuality has come to be regarded as determined almost exclusively by psychic experiences, personality make-up and psychogenic factors. Henry and Galbraith, however, present evidence to show the existence of constitutional and physiologic factors. Their material consisted of thirty-three patients, observed at the Bloomingdale Hospital, who derived pleasure from homosexual experiences (seventeen men and sixteen women). As a control they used five men and ten women whose heterosexual adaptation was reasonably satisfactory. They investigated certain constitutional factors, such as the skeletal heaviness, carrying angle, distribution of fat, muscle contour, distribution of hair, voice, size of the penis and testes, scrotal fold, menses and character of the external female genitalia.

From their tabulations it appears that a small carrying angle, large muscles, deficiency of hair on the chest and face, a high-pitched voice, small genitalia and a persistent scrotal fold were more common in the male homosexual than in the male heterosexual group. Among the women, firm adipose tissue, excess hair on the face and chest, a small uterus and a tendency toward a male distribution of pubic hair were more frequent in the homosexual than in the heterosexual group. A heavy skeleton occurred in a greater proportion of homosexual men than of heterosexual men. The psychosexual histories in the two groups were different. All persons in the control (heterosexual) group were married; they had a total of thirty-eight children; none had been unfaithful after marriage; none were separated or divorced. Only 25 per cent of the homosexual persons were married; none of these had made a satisfactory heterosexual adjustment, three fourths of the marriages having been dissolved by divorce or separation.

All of the heterosexual subjects, as well as all of the homosexual subjects, were patients in a hospital for mental diseases.

DAVIDSON, Newark, N. J.

A NEW CLINICAL FORM OF THE SYNDROME OF THE NASAL NERVE. J. M. V. ORTIZ, Ann. d'ocul. **171**:479 (June) 1934.

Ortiz reports the following case: Marie X., aged 27, an Argentine, married, with a family history of no importance, at the beginning of the year complained that for several days she had had painful and violent orbital and periorbital attacks

on the left side, which were especially localized on a level with the palpebral frontal region and sometimes radiated toward the ala of the nose and toward the temporoparietal region on the same side. At times these attacks were so violent that the patient was unable to sleep. They were accompanied by photophobia, by excessive epiphora and by a painful pricking sensation on a level with the eye on the same side. At that time the conjunctiva was congested, but no secretion was present. There was excessive nasal secretion on the same side as the neuralgic pain. Treatment confirmed the tentative diagnosis of syndrome of the nasal nerve, because following the application of pulverized cocaine and epinephrine to the anterior part of the left nasal cavity all the symptoms disappeared.

The author states that this is the first case reported in which a nasal syndrome with a lesion of the conjunctiva was present without conjunctivitis and without a lesion of the cornea or the iris. Although this new clinical form has not been studied, it has been observed by Charlin. In the majority of cases the etiologic cause of this syndrome is an irritated nasal spur. In the author's case the rhinologist confirmed the fact that there was a deviation of the nasal septum, but Ortiz states that the etiologic factor may be of general origin. Charlin has described interesting cases in which syphilis, diabetes and a buccodental focus of infection are the determining causes of the syndrome of the nasal nerve.

Before applying cocaine and epinephrine it is necessary to make a thorough clinical examination in order to ascertain the general cause of neuritis of the nasal nerve.

BERENS, New York.

PRECIPITATING FACTORS IN MANIC-DEPRESSIVE PSYCHOSES. JOHN H. TRAVIS, Psychiat. Quart. **7**:411 (July) 1933.

Travis reviews a series of seventy cases of manic-depressive psychoses (fifty-three in females and seventeen in male subjects) and classifies them according to the apparent precipitating causes. In each sex group, marital maladjustment was the most frequent cause, accounting for the psychoses of 25 per cent of the male and of 43 per cent of the female patients. Sickness or death in the family was assigned as a causative factor in fifteen of the cases in females and in three of those in males. Other agencies included childbirth, physical ill health, parental antagonism and economic stress. The last-mentioned factor was found to be the cause in 25 per cent of the cases in males and in only 5 per cent of those in females. Travis attempts to explain the development of the psychosis on analytic principles; he believes that a fixation at the homosexual or narcissistic level or a disturbing Oedipus or Electra complex plays a rôle in the large group of maritally maladjusted persons. Expressions of hatred of the spouse, made in dreams, delusions or other forms by many of the patients in this classification, may be considered reflections of the conjugal incompatibility consequent on these psychic disturbances. In the group of patients whose psychosis appears to have been precipitated by death or illness in the family, the underlying mother or father fixation is usually clear. The death of the subconsciously hated parent will produce a feeling of guilt, while the death of the subconsciously adored parent will produce the depression more directly. In 85 per cent of the cases in this group the death was that of a parent. Travis urges that the physicians and social workers who take the patients' mental histories lay more stress on parental relationships and conjugal adjustment.

DAVIDSON, Newark, N. J.

PAPILLARY EDEMA AND ARTERIAL HYPERTENSION. L. RIMBAUD, H. VIALLEFONT, G. ANSELME-MARTIN and R. LAFON, Rev. d'oto-neuro-opht. **12**:414 (June) 1934.

The relations between general arterial hypertension and spinal and retinal tensions are not yet established. A case of arterial hypertension with hypertension of the cerebrospinal fluid and of the retinal artery (pressure of 90 mm.), accompanied by bilateral papillary edema, was thoroughly studied and is reported in

extenso. Spasm of the retinal arteries, cerebral tumor and nephritic retinopapillitis were eliminated as possible causes. It seems that the arterial hypertension was primary and that the other troubles were dependent on it. This observation emphasizes the fact that edema and papillary stasis are not always signs of cerebral tumor. There was also a marked decrease in the arterial tension after lumbar puncture. This phenomenon is not constantly observed; perhaps it is manifested only when the central nervous regulation of arterial tension is disturbed. The observations and experiments of a number of investigators indicate that lesions of certain bulbar, pontile or juxtahypophyseal regions may cause progressive arterial hypertension. As to the relation between general arterial tension and retinal arterial tension, the case brings up the question: Why is there relative hypertension in the domain of the internal carotid artery in cases of essential hypertension? It is tentatively suggested that general arterial hypertension "brings on a hyperdialysis at the level of the choroid plexuses and thus hypertension of the cerebrospinal fluid, the latter provoking an elective reaction of the intracranial arterial system, which is made manifest by retinal arterial hypertension and even papillary stasis at times."

DENNIS, San Diego, Calif.

GENERAL PARALYSIS: NONFEVER TREATMENT BY CEREBRAL LIPOIDS AND TRYPARSAMIDE. EMIL T. HOVERSON, Am. J. Syph. & Neurol. **18**:221 (April) 1934.

Choroschko and his collaborators (ARCH. NEUROL. & PSYCHIAT. **29**:655 [March] 1933) have pointed out that cerebral lipoids may be given to patients with dementia paralytica to fill the gap occasioned by the disintegration of lipoid materials during the disease process. It is known that injections of lipoids given to patients with tuberculosis and syphilis cause the formation of specific antibodies. To test the value of this form of therapy, Hoverson first subjected six patients with dementia paralytica to treatment with lipoids. None of them were suitable for fever therapy because of age or physical condition. One cubic centimeter of a preparation of cerebral lipoids was injected into the gluteal musculature every other day for forty days. Five of the six patients showed marked mental improvement, but little serologic change was noted. By supplementing the lipoid therapy with tryparsamide, however, definite serologic improvement was usually brought about.

The program was repeated with twenty-five patients. Ten injections of tryparsamide (3 Gm. at each dose, once a week) were given, with twenty injections of cerebral lipoids (1 dose: 1 cc., every other day). Of these twenty-five patients, twelve (or 48 per cent) attained sufficient clinical improvement to be paroled from the institution, eight improved somewhat and five did not improve at all. Unlike fever therapy, the treatment is painless and can be administered in the physician's office or in the patient's home. The author considers this form of treatment also the choice in asymptomatic neurosyphilis.

DAVIDSON, Newark, N. J.

OCULAR CHANGES IN CASES OF JUVENILE AMAUROTIC IDIOCY. BENGT ROSENGREN, Upsala läkaref. förh. **3**:151 (Feb.) 1934.

Rosengren reports twenty-seven cases of Spielmeyer-Stock's disease which were studied clinically and pathologically. He states that the ocular changes present a uniform and practically always identical picture in both eyes of the same person. As a rule there is an acute onset between the ages of 5 and 8 years, with rapid loss of vision, leading to complete amaurosis in one year. During the early stages there is a granular appearance of the eyegrounds, especially of the macular region. The retinal vessels soon become narrowed, and the papilla becomes yellowish gray. Later, secondary pigmentation is to be seen in the papilla, which becomes pale. In the more advanced stages there is a greater increase in the amount of pigment, and frequently a posterior cortical cataract develops.

Anatomically, the disease is characterized, as Stock originally described it, by primary degeneration of the cones and rods followed by disintegration of the epithelial pigment cells. In the early stages no notable changes in the internal layers of the retina are to be seen. Later, however, there are pronounced changes, especially in the ganglion cells—changes identical with those in the cerebral ganglion cells. In the most advanced cases there is also atrophy of the optic nerve. Rosengren doubts the possibility of a uniform etiology for the degeneration of pigment. He thinks that there are probably a number of etiologic factors.

The rather large number of cases studied is due to the unusual organization for the care, supervision and study of blind children in Sweden.

NOTKIN, Poughkeepsie, N. Y.

KAHN REACTION WITH SPINAL FLUIDS CONTAINING VARYING AMOUNTS OF SYPHILITIC BLOOD. ADOLPH B. LOVEMAN and LOUISE STOCKING, Arch. Dermat. & Syph. **29**:653 (May) 1934.

Neurologists are frequently puzzled by the problem of evaluating a positive reaction to the Kahn test in blood-tinged spinal fluid. If the Kahn test of the blood is positive, the question of the extent to which the blood serum has influenced the spinal fluid must be answered. To determine this, the authors mixed varying amounts of spinal fluid which gave a negative reaction to the Kahn test with blood serum which reacted positively to the Kahn test and tested the mixture. Using 6 cc. of spinal fluid (known to react negatively to the Kahn test) they discovered great variation in the amount of blood serum necessary to produce a positive reading with the spinal fluid. In some instances as little as one twenty-eighth of a drop of whole blood changed the reaction of the spinal fluid, while in others as much as 8 drops was required. While it is theoretically possible to determine the amount of blood in blood-tinged fluid and thus calculate the reliability of the reaction, this process entails such difficulties as to render it impracticable. The authors therefore suggest that a spinal tap should be repeated when bloody fluid is obtained, and when both the blood and the spinal fluid are found to give a positive reaction to the Kahn test. The authors also point out that the factor producing this serologic change (from negative to positive) in blood-tinged spinal fluid is present in the serum of the blood and not in the erythrocytes.

DAVIDSON, Newark, N. J.

THE EARLY INFANTILE SEXUALITY OF MAN AS COMPARED WITH THE SEXUAL MATURITY OF OTHER MAMMALS. MAX LEVY-SUHL, Internat. J. Psycho-Analysis **15**:59 (Jan.) 1934.

There is evidence that infantile sexuality is a biologic remnant in the course of evolution of man. In one form or another man existed long before the glacial period, and there is reason to suppose that sexual maturity came not in youth but in early childhood between the ages of 4 and 5. To support this theory Levy-Suhl refers to the evidence in the animal kingdom. There he finds that most cattle mature sexually before the age of 12 months. The only animal that matures at an age corresponding to that of maturity in human beings is the elephant; the male matures at the age of 20 years and the female at the age of 16. Histologic evidence shows that the female germ is substantially mature when the child is 5 or 6 years of age, but at this age a pause in development takes place because the rest of the soma of the girl is not ready for conception and reproduction. There is thus a period of latency between early childhood and youth which one also observes psychologically in psychoanalysis. The same biologic forces which operate in man in delaying mature sexuality also operate in the elephant. The elephant is rather unique in the animal kingdom and has practically no relationship to other species. The author believes that the data of mammalian phylogeny support the material which one observes in psychoanalysis.

KASANIN, Howard, R. I.

NEW DEVELOPMENTS IN THE CARE AND TRAINING OF MENTAL DEFECTIVES. CHARLES L. VAUX, Psychiatric Quart. **7**:673 (Oct.) 1933.

Among the newer and more gratifying developments in the care of the feeble-minded Vaux lists: (1) extension of an educational program so that every child may have educational opportunities up to his capacity, avoidance of a chronologic age maximum or mental age minimum as a criterion of admission to the institutional school and placement according to achievement test scores; (2) training classes in domestic arts designed to instruct the patients in service in a small home (to be distinguished from training in an institutional kitchen or bedroom service); (3) occupational therapy on a par with academic work, seasonal, individualized and thoughtfully planned; (4) classes in habit training to make up for the defective habit training supplied by inadequate parents or poor environment; (5) physical training to develop health, grace, coordination, balance and interest; (6) colony houses in the village outside the institution which the inmate may use as a half-way house, in which he may adjust himself gradually to community life and in which he may find a social center and a source of help and advice, and (7) boarding in private families. These developments give increasing hope of returning many defective persons as assets to a community in which they had formerly been nuisances, liabilities or menaces.

DAVIDSON, Newark, N. J.

EVOLUTION OF THE AVERAGE RETINAL ARTERIAL DIASTOLIC BLOOD PRESSURE COMPARED WITH THE SPINAL FLUID PRESSURE AFTER LUMBAR PUNCTURE. A. MAGITOT and A. DUBOIS, Ann. d'ocul. **170**:535 (June) 1933.

Lumbar puncture profoundly modifies the pressure equilibrium of the cerebrospinal fluid. The changes are reflected in the retinal arterial blood pressure. In three cases the needle with which the lumbar puncture was made was left in place for a half hour, and the pressure was measured every five minutes. Thus a graph of comparative curves showing the variations was made. The spinal fluid pressure decreased during decompression but increased soon afterward; after a quarter of an hour it remained constant. The retinal diastolic blood pressure varied in the same way; it decreased and increased as the spinal fluid pressure did. In one case the decrease of retinal blood pressure was prolonged after lowering the spinal fluid pressure, but in the end it had the same variations. The variations of the retinal arterial tension were not proportionate to the variations in the spinal fluid pressure. There is a qualitative rather than a quantitative similarity between the two pressures. The average pressure taken at the first emptying of the artery was constantly 10 below the diastolic pressure along the entire length of the curves.

BERENS, New York.

LARYNGEAL PARALYSES FOLLOWING INJECTION OF THERAPEUTIC SERUM. H. ROGER, PREVOT, WAHL and BREMOND, Rev. d'oto-neuro-opht. **12**:419 (June) 1934.

Two cases of laryngeal paralysis following the injection of antitetanic serum are reported. In the first case the paralysis involved the dilator muscles of the glottis and the soft palate and appeared seven days after the injection; serum sickness developed and was followed within a few hours by the paralysis. Syphilis was definitely eliminated, and no cause other than the effect of the serum could be discovered. Nervous accidents following various forms of serum therapy are known. The paralyses are usually located in the brachial plexus but may be of polyneuritic type; it is exceptional for the reaction to be localized in one or two cranial nerves. In this case the lesion is assumed to be in the bulbar nuclei of the tenth and eleventh nerves or their intrabulbar fibers. In the second case the right vocal cord and the aryteno-epiglottic muscle were involved, paralysis of the right superior and inferior laryngeal branches resulting. In spite of repeated and thorough examinations, no cause other than the serum sickness could be elicited. The only similar cases known to the writers are one reported by Lavrand and one reported by Schauwecker.

DENNIS, San Diego, Calif.

ON THE PHYSIOLOGY OF MICTURITION. D. DENNY-BROWN and E. GRAEME ROBERTSON, Brain **56**:149 (July) 1933.

The history of the study of the physiology of micturition shows considerable variation in opinion as to the sequence of events in normal human micturition. A method is described by which records of the vesical pressure may be obtained during manipulations of the volume of the bladder and during micturition. It is shown that the human bladder reacts to distention by contraction of its wall. Willed effort to micturate can evoke powerful contractions of the bladder, with very brief latency of development. Sensation is only indirectly related to pressure, and the increase in area of the vesical wall markedly lowers the threshold at which added spontaneous active contractions can produce sensation. The primary factor in discharge is contraction of the wall of the bladder with an accompanying secondary reciprocal relaxation of both sphincters. The important question of determining the means by which the bladder and sphincter, which possess a definite measure of autonomy, are subjugated to the control of the will is discussed. A careful reading of this paper is necessary in order to reach some understanding of this complex process.

MICHAELS, Boston.

SURGICAL TREATMENT OF INTRACTABLE PAIN. LOYAL DAVIS, J. A. M. A. **101**:1921 (Dec. 16) 1933.

The author states that visceral afferent painful impulses travel by way of the splanchnic nerves to the spinal cord and thence upward by relays of short neurons in the gray matter. Chordotomy, unless the lesion is deep and injures the gray matter, will not relieve visceral pain, although it will abolish intractable somatic pain. Section of the posterior roots in which a sufficiently large number of roots are severed will abolish visceral pain. The pain of angina pectoris has been abolished by this method. Such an operation definitely attacks the afferent pathway for the painful impulses and does not interfere with the cardiac accelerator mechanism. The stimulation of efferent sympathetic fibers produces changes in the periphery, which in turn stimulate the ordinary somatic afferent fibers that transmit pain. The relief from pain by section of sympathetic fibers is, therefore, based on the interruption of efferent pathways. Section of all the posterior roots that supply the upper extremity in man and in animals interrupts all forms of superficial or deep sensation. There is no evidence of a sensory pathway through the anterior spinal roots.

EDITOR'S ABSTRACT.

THE FASTING BLOOD SUGAR IN SCHIZOPHRENIA. WILLIAM FREEMAN, with the technical assistance of ELLA K. RUGGLES, Am. J. M. Sc. **186**:621 (Nov.) 1933.

A review of the literature shows that of 620 patients, 79 per cent had a normal blood sugar content, 9 per cent showed hypoglycemia and 15 per cent showed hyperglycemia. The present study was made on 59 men with schizophrenia with an average age of 31 years and an average period of hospitalization of about five years. In 95 per cent of 347 determinations the values were within the conventional normal range of 80 and 120 mg. per hundred cubic centimeters. The average value was 96.6 mg., as compared with an average of 95.4 mg. in 31 normal control subjects. The gradual small drop in the average blood sugar level from period to period suggested that habituation played a part in determining this level. There was no relationship between the depth of the psychosis, the age of the patient and the period of hospitalization. It is concluded that schizophrenia is characterized by normal fasting blood sugar levels, but that the individual variability is somewhat greater than in normal subjects.

MICHAELS, Boston.

CERTAIN PARTICULARS OF LABYRINTHINE REACTIONS IN THREE CASES OF TRAUMATIC TEMPORAL LESIONS. G. PORTMANN and P. DELMAS-MARSALET, Rev. d'oto-neuro-opht. **11**:23 (Jan.) 1933.

In an attempt to clear up some obscure points in the cerebral terminations of the vestibular pathways, three cases of injury to the temporal region are reported. Many writers attribute anomalies in the vestibular reactions in cases of cerebral tumor to the secondary effects of hypertension. In traumatic lesions such an explanation cannot be valid. In all three cases vestibular disturbances appeared some years after the injury; in one they were accompanied by epileptic attacks and deafness, and in two caloric and rotatory tests gave normal reactions. In one case there was spontaneous deviation in walking with dissociation in the results of the rotatory and caloric tests. In the other two cases, after rotation to the right, deviation in walking was to the left, and after rotation to the left, deviation was to the right, constituting an inverse reaction. The test of provoked deviation in walking was evidently not made in the first case.

DENNIS, San Diego, Calif.

IPSILATERAL REPRESENTATION IN THE MOTOR AND PREMOTOR CORTEX OF MONKEYS. PAUL C. BUCY and JOHN J. FULTON, Brain **56**:318 (Sept.) 1933.

This paper deals with the locus of the ipsilateral response, the character of the movement which it evokes and the course of the nerve pathways involved. In twenty-one of twenty-seven primates, faradic stimulation of the cortex in a restricted region about the superior precentral sulcus resulted in ipsilateral responses in the extremities. Appropriate hemisection of the spinal cord, which abolishes contralateral response, shows the independence of the ipsilateral response. The ipsilateral response is mediated by a pathway which is entirely ipsilateral. The motor or premotor area of one hemisphere is sufficient to integrate movement in all four extremities, but on removal of areas 4 and 6 from both hemispheres the animal becomes helpless. Clinical reports are cited which suggest that in man the cerebral hemispheres are capable of ipsilateral innervation, but it may not be as extensive as in monkeys. The pathway in man may be identical with that present in the other primates.

MICHAELS, Boston.

SPIROCHETAL FINDINGS IN THE BRAINS OF PARETICS TREATED WITH MALARIA. NICHOLAS KOPELOFF and NATHAN BLACKMAN, Am. J. Psychiat. **13**:19 (July) 1933.

The brains of thirty-nine patients with dementia paralytica who had been treated with malaria and of ten who had not been so treated were examined exhaustively for spirochetes by the Jahnel technic. Spirochetes were found in eight of ten subjects not receiving malaria and in only six of the thirty-nine treated with malaria. Of the six in the latter group, three, who had died within a month of inoculation, showed degenerate forms only. The organisms found in the group not receiving malaria were more abundant than those in the group treated with malaria while degenerate forms were seldom seen in persons who had been treated with drugs only. These findings lead Kopeloff and Blackman to conclude that artificially induced malaria of sufficient intensity will destroy the organisms or, failing to destroy them, will alter the morphology of the spirochete sufficiently to produce degenerate forms.

DAVIDSON, Newark, N. J.

OBSERVATIONS ON THE PARALYSED BLADDER. GORDON HOLMES, Brain **56**:383 (Dec.) 1933.

Thirty patients in whom injuries involved all regions of the spinal cord from the highest cervical segments to the cauda equina were studied with a special technic. In the first phase through which the bladder, paralyzed by a complete lesion of the spinal cord, passes, it behaves as an inert elastic bag with no tendency

to adapt itself to its contents. The second phase occurs two or three weeks after the onset of the paralysis, and is characterized by an increasing resistance to the introduction of fluid and a regaining of some tone. The third phase is distinguished by the occurrence of sudden contractions of the bladder, producing increases of intravesical pressure. It is concluded that the evacuation of the bladder which follows stimulation of the lower limbs is not part of a "mass reflex" and that impulses arising from the periphery of the limbs do not spread to the spinal vesical mechanisms. Under these circumstances micturition is a result of the associated spasm of the abdominal muscles.

MICHAELS, Boston.

JUVENILE DELINQUENCY A PRODUCT OF THE HOME. T. EARL SULLENGER, J. Crim. Law & Criminol. **24**:1088, 1934.

The family is the prime determiner of social behavior. From it comes youth indelibly stamped with noble aspirations or with low, vile antisocial attitudes toward life. The family today is less stable than it has been at any time since the beginning of the Christian era. Out of this situation comes much juvenile delinquency. Burt's study in London showed that 60 per cent of the delinquents studied came from broken homes. The results of a study of two groups of delinquents in Omaha are summarized in the tables. One table shows that in one group 50.7 per cent of the delinquents were from broken homes; the other table is presented to show the percentage of delinquents from the various types of broken homes. This leads to the inevitable conclusion that the broken home all too frequently is a breeding place for the criminals of tomorrow; it behooves society to remedy this condition and thus remove one of the chief groups of determinants of juvenile delinquency.

SELLING, Chicago.

EXUDATIVE RETINITIS OCCURRING IN ARTERIAL HYPERTENSION. A. DUBOIS, Ann. d'ocul. **171**:138 (Feb.)) 1934.

Dubois believes that the relation of disturbances of the kidney to retinitis is not clear. Although arterial hypertension is the most frequently associated factor in retinitis, it does not explain the etiology of the disease. Arterial hypertension apparently creates retinitis through circulatory disturbance of the retina, which is frequently associated with intracranial hypertension. Decompression has brought about cure of the local condition in many cases of retinitis, but it has little effect on the general condition. In spite of these facts, the rôle of intracranial hypertension in retinitis is still obscure. Retinitis is not a specific disorder of a specific condition; different factors can produce it, as it is a specific reaction of retinal tissues. The question of the cause of retinitis remains extremely complicated. Certain facts support some theories, and the author hopes that more experimental work will be done, completely renovating the old conceptions of this disease.

BERENS, New York.

TYPHOID VACCINE IN THE TREATMENT OF CHOREA. AARON CAPPER and EDWARD L. BAUER, Am. J. M. Sc. **186**:390 (Sept.) 1933.

The method of treatment employed consisted of the injection intravenously of a mixture of typhoid, paratyphoid A and paratyphoid B vaccine, each cubic centimeter containing 500,000,000 typhoid organisms and 250,000,000 each of paratyphoid A and B organisms. The initial dose was from 0.15 to 0.2 cc. The usual rise in temperature was to between 102 and 104 F. Injections, with increasing amounts of 0.1 cc., were continued daily, usually for six or seven days. Twenty-three patients were studied, the average age being 8½ years; nine (40 per cent) suffered from chronic chorea (duration, four and one-half years). Of the twenty-three patients, nineteen were entirely well at the time of discharge from the hospital. Of those with chronic chorea, eight became entirely symptom-free. The authors were impressed by the marked rapidity with which the symptoms disappeared following the injection of the vaccine.

MICHAELS, Boston.

ANTERIOR LOBE PITUITARY EXTRACT IN THE TREATMENT OF ALOPECIA. LLEWELLYN WILLIAMS LORD, Arch. Dermat. & Syph. **28**:381 (Sept.) 1933.

Fourteen volunteers, all men, suffering from seborrheic alopecia in fairly advanced stages, received a course of treatment with anterior lobe pituitary extract. The drug was given hypodermically, 1 cc. at a time, for 100 injections. Each subject also ingested 10 grains (0.65 Gm.) of the extract by mouth daily. At the end of the treatment, careful measurements in eleven cases showed no improvement, and in some instances the loss of hair had continued to progress. Three of the volunteers displayed some increase in the formation of the lanugo hair. These three subjects received a second course of 100 injections, but no further growth of hair appeared. Five patients with alopecia areata were also studied; three of these received injections of the pituitary extract, with good results. Ultraviolet irradiation was found effective in the fourth case, and local application of cresol, U. S. P., and alcohol, in the fifth case. DAVIDSON, Newark, N. J.

THE LOCALIZING SIGNIFICANCE OF SPASTICITY, REFLEX GRASPING, AND THE SIGNS OF BABINSKI AND ROSSOLIMO. MARGARET A. KENNARD and JOHN F. FULTON, Brain **56**:213 (July) 1933.

From previous experiments it is stated that the presence of spasticity in the chimpanzee, and probably in man, has definite localizing value in the study of cortical lesions. The present article is based on the study of four chimpanzees. When area 4 of Brodmann is removed, there are contralateral flaccid paralysis, the Babinski response and diminution of the tendon reflexes. When area 6 is removed, there are contralateral spastic paresis, forced grasping, increased tendon reflexes, the Rossolimo response and fanning of the toes. The first type of response suggests a lesion restricted to the pyramidal tract, while the second type points to lesions involving the premotor area or its projection system from the cortex.

MICHAELS, Boston.

FOUR CASES OF SYMPATHOMA OF THE SUPRARENAL CAPSULE WITH OCULAR SYMPTOMS. VAN DER STRAETEN and MALDAGUE, Ann. d'ocul. **170**:905 (Oct.) 1933.

In this report four cases of sympathoma of the medullary part of the suprarenal capsule are added to forty cases published in the literature to show that the disease is not so rare as it is generally considered. Exophthalmos, the most marked ocular symptom, is often seen early and is the first symptom to attract attention to the nature of the disease. It is due to metastasis in the bones of the orbit, forcing the eyeball forward. Tumors are generally visible on the surface of the skull. The diagnosis is confirmed by a biopsy, practiced preferably on a tumor of the bones of the skull or on a ganglion. The primary tumors and the metastases (especially of the bones) are formed of cells of embryonic character; the nuclei are deeply stained and the cytoplasm is scanty. Characteristic roset forms are sometimes seen.

BERENS, New York.

CYSTIC OLIGODENDROGLIOMAS OF THE CEREBRAL HEMISPHERES AND VENTRICULAR OLIGODENDROGLIOMAS. J. GODWIN GREENFIELD and E. GRAEME ROBERTSON, Brain **56**:247 (Sept.) 1933.

Since 1926, the authors have found only 9 oligodendrogliomas in a series of 230 cerebral gliomas. Five of them are described, of which 3 were cystic tumors of the cerebral hemispheres and 2 were midline ventricular tumors. Contrary to the findings of Martin (*Brain* **54**:330, 1931), no age distinction was made between laterally and medially placed tumors. The 2 patients with midline tumors had long preoperative histories. Of pathologic interest are the alteration of tumor type from a typical and easily recognizable oligodendroglioma to a reticular tumor

containing mucinoid substance in its meshes and the character of the stroma or reticulum, which may give rise to a mucinoid exudate which may form large accumulations.

MICHAELS, Boston.

THE EFFECT OF ACTIVITY ON THE FORM OF THE MUSCLE TWITCH. J. L. PARKINSON, J. Physiol. **78**:106 (April 13) 1933.

Parkinson points out that during a series of muscle twitches at intervals of a second or two a considerable spreading out of the contraction occurs. Recovery, which is independent of the presence of oxygen, is complete within a minute. The spreading out is not connected with the formation of lactic acid, nor is the recovery associated with restoration of phosphagen, since both occur unchanged in muscles adequately poisoned with iodo-acetate. A complete resting condition (absence of stimulation with previous intact circulation) delays the spreading out, but its onset is not quickened by circulatory stoppage during the series. Sarforii showed the same phenomenon. "Fatigue" is not the cause of it, since usually the response increased during a series. Temperature and p_H have no effect on it. Its relation to known chemical changes in muscle is not obvious. ALPERS, Philadelphia.

CHRONIC ADRENAL INSUFFICIENCY: A HITHERTO UNDESCRIBED SYNDROME: WITH CASE REPORT. MAURICE PACKARD and H. F. WECHSLER, Am. J. M. Sc. **186**:66 (July) 1933.

The authors report a case in which the outstanding clinical features were extreme emaciation, with complete loss of body fat, asthenia, anorexia, polyneuritis, trophic ulcers, with absence of pigmentation, hypotension and edema. At autopsy there was found an advanced degenerative lesion of both adrenal glands, with necrosis, regeneration, hemorrhages and capillary and venous thromboses. The edema was considered to be of the malnutritional type. The present condition is compared to the state of chronic adrenal insufficiency produced in animals by bilateral adrenalectomy. The effects of total and partial inanition and the various vitamin deficiencies on the adrenal glands in both animals and man are discussed.

MICHAELS, Boston.

PARALYSIS OR CONGENITAL ABSENCE OF ACCOMMODATION IN THREE BROTHERS. J. SEDAN and A. ROUX, Ann. d'ocul. **170**:891 (Oct.) 1933.

Three young brothers who had no accommodation and were able to read only with a $+4$ diopter convex lens were observed. They were not hyperopic, and therefore, vision for distance was diminished by convex lenses of $+0.75$ diopter. There was no family history of syphilis and no history of diphtheria or diabetes. Neurologic examination gave negative results. A sister was normal. All ocular functions were normal except that there was paralysis of accommodation and the reflex to convergence and accommodation was absent. Atropine and physostigmine (eserine) had no effect on accommodation. As the motility of the iris was normal, failure of accommodation seemed to be due to aplasia of the ciliary muscle rather than to a partial congenital paralysis of the third nerve.

BERENS, New York.

THE RACIAL FACTOR IN PERNICIOUS ANEMIA: A STUDY OF FIVE HUNDRED CASES. RICHARD D. FRIEDLANDER, Am. J. M. Sc. **187**:634 (May) 1934.

From an analysis of the cases of 500 patients with pernicious anemia (from a total of 80,415 patients admitted to the Peter Bent Brigham Hospital), the evidence is in favor of the view that the predisposition to this disease is racial as well as constitutional and familial. The condition is largely confined to persons endowed with a diathesis characterized by a fair complexion, light hair, blue eyes and

achlorhydria. The color of the irides was recorded in only 66 of the 500 cases and was found to be blue in 72.7 per cent. The causes of death in 15 cases of proved pernicious anemia in which adequate liver therapy had been administered indicated that there was no relation to the anemia and that death was essentially due to conditions met with in ordinary people of the same age. MICHAELS, Boston.

SYMPTOMS OF TRAUMATIC PROGRESSIVE PARALYSIS. G. BOSCHI, A. CHEDINI and F. BARISON, Ann. d'ocul. **170**:708 (Aug.) 1933.

Boschi, Chedini and Barison report a case of progressive paralysis in which the symptoms appeared immediately after trauma. They point out that the "diagnosis of a short circuit" (psychic disturbances caused by trauma) suggested craniectomy to the surgeon. The following clinical course showed that there had been no indication for craniectomy and that the neurologic signs then present actually contraindicated surgical intervention. The authors believe that they may attribute to progressive traumatic paralysis a characteristic symptomatology consisting of contralateral jacksonian epileptiform seizures, contralateral symptoms of involvement of the pyramidal tract and a tumultuous course, with polymorphonucleosis in the cerebrospinal fluid in the early stages. BERENS, New York.

A MEASURE OF DELINQUENCY. A. R. GILLILAND and J. C. EBERHART, J. Crim. Law & Criminol. **24**:736 (Nov.-Dec.) 1933.

This paper is a report of the application of H. R. Laslett's word association test for delinquency, which was given to 546 Chicago boys who were selected so as to represent widely varied social gradations. The primary value of such a test is in the prevention of delinquency. Laslett's results indicated that this technic may be expected to pick out potential delinquents from an unselected group. Results from the application of the test to the Chicago boys, however, did not confirm this prediction, and the question of the relative influences of social delinquency and of social and economic levels on the scores obtained with the association test remains unanswered. SELLING, Joliet, Ill.

DOUBLE PARALYSIS OF THE EXTERNAL OCULOMOTOR NERVE IN A DIABETIC PATIENT. VILLARD, VIALLEFONT and BOUZIGUES, Rev. d'oto-neuro-opht. **12**:425 (June) 1934.

A patient, aged 51 at the time of examination, twenty years previously had suffered from frequent crises of ophthalmic migraine, with left hemianopia and vomiting, but for several years he had been free from attacks. Examination revealed bilateral paralysis of the sixth nerves and diabetes. The paralysis of the right side lasted only a few weeks. Signs of diabetic pseudotabes were present. The suggestion is made that miopragia of the nervous system, perhaps even vascular spasm, played a rôle in the pathogenesis. DENNIS, San Diego, Calif.

THE CLINICAL SIGNIFICANCE OF THE ANTERIOR CHOROIDAL ARTERY. A. A. ABBIE, Brain **56**:233 (Sept.) 1933.

The variations of the anterior choroid artery must be considered from its double origin, one part arising from the cranial division of the internal carotid artery to supply the paleostriatum and the pyriform cortex, the other from the caudal division to supply the remainder of the anterior choroidal field. The phylogenesis of the artery is discussed to help solve the problem of its variation. The field of major clinical importance is the terminal area of distribution, which is least affected by variation. Proved cases of occlusion of the anterior choroid artery are rare. The clinical features are hemiplegia, hemianesthesia and hemianopia, all toward the side opposite the lesion. MICHAELS, Boston.

MODIFICATIONS OF THE NASAL MUCOUS MEMBRANE FOLLOWING CERVICAL SYMPATHECTOMY: HISTOLOGIC AND EXPERIMENTAL STUDY. R. MOTTA, Ann. d'ocul. **170**:701 (Aug.) 1933.

Motta observed the nasal cavities after removal of the cervical sympathetic nerve in young rabbits (about 24 days old). He concludes that when the superior ganglion has been removed, unilateral sympathectomy provokes primarily (after eighteen hours) vasodilatation in the nasal mucous membrane of the opposite side and later a mild homolateral syndrome. Twenty-eight days after the simultaneous removal of the cervical sympathetic nerves on both sides, the mucous membrane on one side is velvety and the vessels are dilated, and the mucous membrane on the other side is ischemic and shrunken.

BERENS, New York.

EXPERIMENTAL CATATONIA INDUCED BY BULBOCAPNINE. B. FERNANDES and F. FERREIRA, Encéphale **28**:445 (June) 1933.

Experimental work led the authors to the following hypothesis and conclusion: Bulbocapnine in moderate doses provokes, among vertebrates, a syndrome of akinesia, passivity and catalepsy. In high doses it provokes hyperkinesia, convulsions and death. These two aspects of the effects of the drug have been noted in lower animals devoid of a neocortex. The similarity of catalepsy induced by bulbocapnine to "spontaneous" catatonia is close. It seems possible that the action is explained by the liberation of a preformed mechanism which conditions the reflexes of immobilization. Thus, under ordinary circumstances, this reflex is inhibited from centers on which bulbocapnine exercises a paralyzing action.

ANDERSON, Los Angeles.

ELECTROMYOGRAPHIC RECORDS OF MUSCLE TREMORS AND PHONOMYOGRAPHIC RECORDS OF MUSCLE MURMURS IN POSTENCEPHALITIC PARKINSON'S DISEASE AND ESSENTIAL TREMOR. HARRY L. SMITH, EDWARD J. BOLDES and CHARLES SHEARD, Am. J. M. Sc. **186**:518 (Oct.) 1933.

Muscle murmurs were studied in eight cases of postencephalitic Parkinson's disease and in one case of essential tremor. The murmurs in the former cases occurred rhythmically and at an average rate of 350 each minute. It is believed that the muscle murmurs and sounds are due to extreme tautness of the muscles and that a few fibers are contracting somewhat rhythmically to produce the sounds. The murmurs could be heard readily with the unaided ear.

MICHAELS, Boston.

DIAGNOSIS OF EXTRADURAL TUMORS OF THE SPINAL CORD. G. FUMALORA and C. ENDERLE, Ann. d'ocul. **170**:705 (Aug.) 1933.

Fumalora and Enderle suggest clinical and roentgenologic criteria which may aid in the diagnosis of extradural tumors of the spinal cord. Extreme violence and considerable increase in root pains, few symptoms of compression of the spinal cord and pain on pressure on the spinous apophyses corresponding to the localization of the lesion make up the clinical picture. The roentgenographic picture, following the injection of iodized poppy-seed oil 40 per cent, shows a shadow like a "cap of liberty" in a reversed triangular projection (base upward) and in another projection at right angles to the first; there is a difference between the diameters of the shadow in the two projections.

BERENS, New York.

THE CLINICAL PICTURE OF BROMIDE POISONING. E. B. CRAVEN, Am. J. M. Sc. **186**:525 (Oct.) 1933.

A composite picture is presented of the clinical state in eight cases of bromide poisoning alone, uncomplicated by a confusing psychiatric basis. The usual seda-

tives do not allay, but rather seem to augment the excitement. Sodium chloride, up to 2 Gm., is given by mouth every two hours, with a daily intake of from 6,000 to 8,000 cc. of fluid. After the intravenous administration of sodium chloride the bromide level of the blood decreases, along with a greatly increased urinary excretion of bromide. It is suggested that a distinct parallel exists between the bromide levels in the blood and spinal fluid and the clinical condition of the patient.

MICHAELS, Boston.

BINASAL HEMIANOPIA IN A CASE OF POSTHEMORRHAGIC BLINDNESS. E. HARTMANN, Ann. d'ocul. **170**:712 (Aug.) 1933.

Hartmann observed a man 58 years of age who after an illness of three days with violent hematemesis became completely blind. There was spontaneous improvement of vision for six weeks, after which there was no change. Six months later, atrophy of both disks with contraction of the arteries was observed. The patient was able to count fingers with the right eye; vision in the left eye was 1/50. The visual field showed binasal hemianopia. In spite of treatment with acetylcholine hydrochloride and *rhodargyl*, no change occurred. It is difficult to localize the lesion and to determine its pathogenesis.

BERENS, New York.

SEPARATE SECRETORY AND VASODILATOR FIBERS IN THE CHORDA TYMPANI. A. v. BEZNÁK, Arch. f. d. ges. Physiol. **233**:155, 1933.

Secretion of saliva and vasodilatation were produced independently from each other by stimulation of the chorda tympani. In the normal chorda a stronger alternating current was necessary to produce secretion than to produce vasodilatation. After partial degeneration of the chorda the vasodilator fibers lost their excitability earlier than the secretory fibers; then, weak currents stimulated the secretion without changing the flow of blood in the gland. The inference is drawn that the chorda has two groups of nerve fibers: secretory and vasodilator fibers.

SPIEGEL, Philadelphia.

LIPOMA IN THE CEREBELLOPONTILE ANGLE AS AN ACCESSORY FINDING IN TUBERCULOUS MENINGITIS. H. STEFAN, Ztschr. f. d. ges. Neurol. u. Psychiat. **145**:445 (April) 1933.

Stefan reports the occurrence of a lipoma in the cerebellopontile angle in a case of tuberculous meningitis. The tumor, on the left side, was the size of an olive and was soft and yellow. Microscopically, it was a typical lipoma. The course of the tumor was symptomless. Mention is made of a case reported by Wohlbach and Millet of two small tumors in the cerebellopontile angle and a large lipoma extending the entire length of the spinal cord under the dura.

ALPERS, Philadelphia

INTRACRANIAL ANEURYSM OF THE RIGHT INTERNAL CAROTID ARTERY, MADE VISIBLE BY ARTERIOGRAPHY. EGAS MONIZ, Rev. d'oto-neuro-opht. **11**:746 (Dec.) 1933.

A case of aneurysm of the internal carotid artery within the skull, the diagnosis of which was possibly only by arteriography, is reported. The only symptoms were headaches and noises in the head, which were more noticeable on the right side. Three injections of thorium dioxide were necessary, two being made into the common carotid artery and the third into the internal carotid. An excellent reproduction of the roentgenogram accompanies the article.

DENNIS, Colorado Springs, Colo.

DYSMENORRHEA RELIEVED BY RESECTION OF PRESACRAL SYMPATHETIC NERVES. A. W. ADSON and J. C. MASSON, J. A. M. A. **102**:986 (March 31) 1934.

Adson and Masson report six cases of dysmenorrhea relieved by section of the presacral nerve by the method described by Cotte in 1924. The group of cases reported is too small to permit general conclusions, but the results obtained are so satisfactory that it seems justifiable to the authors to employ the procedure for patients suffering from dysmenorrhea who cannot be relieved by medical measures such as endocrine therapy, the administration of tincture of belladonna, occasional doses of codeine, catharsis or hot douches at the onset of the menstrual periods.

EDITOR'S ABSTRACT.

THE BIOLOGIC CONCEPTION OF SLEEP. A. JANICHEWSKI, Encéphale **28**:184 (March) 1933.

Janichewski contends that sleep must be looked at as a force essentially biologic, and thus operating either from within or without the individual organism. It is not proper to speak of special centers for sleep. Sleep should not be viewed as a state of repose of the organism. It is an active process which has for its goal the arrest or diminishing of activity toward the external world, and the promotion of the vital internal activities. Psychic activities during sleep are directed toward the elaboration or remodeling of previously received impressions.

ANDERSON, Los Angeles.

LEIODYSTONIA, AN ENDOCRINE-AUTONOMIC NEUROSIS OF THE TROPICS. P. M. VAN WULFFTEN PALTHE, Brain **56**:479 (Dec.) 1933.

Leiodystonia is a latent constitutional inferiority characterized by a disturbance in the regulation of the functions of the vegetative system and especially by a lability in the tonus of the involuntary muscles. Symptoms which present themselves in ocular, intestinal, circulatory and cerebral manifestations, together with the mental and physical abnormalities, should be regarded as a whole. Citations of differences in carbon dioxide tension, body temperature, basal metabolic rate and blood pressure are presented to show that there is a greater lability of the functions of the vegetative system in tropical climates.

THE EFFECT OF PITRUITRIN INJECTIONS ON BLOOD PRESSURE IN MAN. W. M. MOFFAT, Am. J. M. Sc. **186**:854 (Dec.) 1933.

This study was undertaken to determine if there was any constant effect following the intramuscular injection of 1 cc. of solution of pituitary into man. The findings in sixty-two persons from 8 to 56 years of age showed that there were no constant changes in the blood pressure, and the general trend of the blood pressure was downward rather than upward. There was a slight but constant decrease in pulse pressure. In the hypertensive group (three patients) the fall in the systolic pressure was more marked and immediate than in the normal and hypotensive groups.

OBSERVATIONS ON THE ETIOLOGICAL RELATIONSHIP OF SEVERE ALCOHOLISM TO PELLAGRA. TOM D. SPIES and H. F. DE WOLF, Am. J. M. Sc. **186**:521 (Oct.) 1933.

In sixty-two of seventy-three cases of pellagra a history of severe alcoholism was obtained. Ten patients with pellagra received an adequate diet, yeast and large quantities of whisky, and recovered. The following hypothesis is suggested: that severe alcoholic imbibition by some persons causes inadequate ingestion of food, and that this predisposes to the development of pellagra because the person utilizes the calories in the alcohol instead of an adequate diet. It is further suggested that alcoholic pellagra is a form of true (endemic) pellagra.

MICHAELS, Boston.

THE METABOLIC COST OF SUSTAINED POSTURES IN NORMAL AND CATATONIC SUBJECTS. J. B. GAYLOR and G. M. WISHART, Brain **56**:282 (Sept.) 1933.

The energy exchange under basal conditions and during maintenance of a fixed posture was investigated in three patients with catatonia and in five normal subjects. A definite increase of metabolism while in the fixed posture was observed in both the normal and the pathologic subjects. The posture was maintained at a cost approximately one-fifth less in the psychotic than in the normal persons. The pulse rate, systolic pressure and diastolic pressure were much less disturbed in the patients than in the healthy subjects.

ON A CORTICAL FLEXOR TONE IN THE FORE-LIMB OF THE CAT, WITH OBSERVATIONS ON THE HEMIPLEGIC ATTITUDE IN MAN. D. M. BLAIR and R. J. S. MCDOWALL, Brain **56**:99 (March) 1933.

During the course of anesthetizing cats it was observed that prior to the stage of quadrupedal extension (resembling decerebrate rigidity) a phase occurred in which the hindlimbs were rigidly extended while the forelimbs were rigidly flexed and adducted. This tonic flexor position of the forelimb was abolished by removal of the contralateral motor area and a considerable extent of the adjoining cortex. The relationship of these observations to the human hemiplegic posture is discussed.

PELLAGRA; IMPROVEMENT WHILE TAKING SO-CALLED "PELLAGRA-PRODUCING" DIET. TOM DOUGLAS SPIES, Am. J. M. Sc. **184**:837 (Dec.) 1932.

The patients in six typical cases of pellagra, four of whom had mild mental symptoms, received a pellagra-producing diet, i. e., one in which vitamins D, C and G were restricted. The cutaneous lesions in five cases improved strikingly; dementia and a burning sensation of the feet did not improve. Although interpretation is hindered by many unknown factors, it is suggested that there is a secondary factor in the production of pellagra, perhaps analogous to the gastric defect of pernicious anemia.

THE ADVANTAGE OF INTRAMUSCULAR INJECTIONS OF A SOLUTION OF LIVER EXTRACT IN THE TREATMENT OF PERNICIOUS ANEMIA. WILLIAM P. MURPHY, Am. J. M. Sc. **186**:361 (Sept.) 1933.

The conclusions in regard to the advantages secured by the intramuscular injection of liver extract are: (1) certain dosage; (2) rapid effect in severe relapses, resistant cases, combined system disease and uncomplicated pernicious anemia; (3) economy; (4) greater facility in travel. It has a minor disadvantage, that of the mode of administration by means of a needle.

THE RATE OF CONDUCTION AND REFRACTORY PERIOD OF THE HUMAN SENSORY NEURONE. F. GOLLA and S. ANTONOVITCH, Brain **56**:71 (March) 1933.

A method is described for the investigation of certain functions of the sensory portion of the nervous system in man. The refractory period in the ulnar nerve was determined; the total refractory period lasted 1.7 sigma, and the partial refractory period, 2.3 sigma. The mean velocity of conduction in the ulnar nerve was found to be 75 meters per second (about twice the velocity of the motor nerve).

MICHAELS, Boston.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTIONS OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, May 8, 1934

CLARENCE P. OBERNDORF, M.D., *President, in the Chair*

ABSCESS OF THE BRAIN: RECOVERY FOLLOWING THE USE OF THE MOSHER DRAIN. DR. ABRAHAM KAPLAN (by invitation).

It seems worth while to present two cases of abscess of the brain in which recovery occurred following the same method of treatment—the Mosher drain (Mosher, H. P.: *Surg., Gynec. & Obst.* **23**:740 [Dec.] 1916). The technic follows: A large exposure of dura is made over the site of the abscess, and the dura is sealed off at the margin of the bone with the Bovie machine; a needle is then introduced into the abscess, and when pus begins to escape the stylet of the needle is quickly replaced to prevent the abscess from emptying itself. A core of dura, overlying brain and wall of the abscess is removed with the aid of the Bovie scalpel, this being an application of King's principle of "uncapping" (King, J. E. J.: *Surg., Gynec. & Obst.* **39**:554 [Nov.] 1924) the wall of an abscess of the brain to allow it to herniate. The lubricated drain is inserted into the abscess cavity, the obturator is removed, and pus is allowed to escape freely. In time the abscess everts itself and spontaneously discharges the drain.

CASE 1.—An Italian shoemaker, aged 39, who entered the Brooklyn Jewish Hospital on Aug. 5, 1933, had had a purulent discharge from the right ear since the age of 8 years. He was well until one month before admission, when he began to have severe frontal and vertical headaches and pain radiating to the right side of the face and teeth. Shortly thereafter, while on his way to work he suddenly had a dizzy spell which caused him to return home. Nausea and vomiting occurred frequently during the next few weeks, and vision began to fail.

On admission the patient was mentally sluggish, spoke slowly and yawned frequently; he complained of frontal headache. The temperature was 99 F., and the pulse rate, 60. There was a purulent discharge from the right ear. On the next day the neck was slightly stiff. The Kernig and Brudzinski signs were present bilaterally. The vessels of the right ocular fundus seemed full.

Laboratory study revealed a leukocyte count of 12,300 with 80 per cent neutrophils. The spinal fluid was under 380 mm. of pressure and contained 160 cells per cubic millimeter, all polymorphonuclear; the Wassermann and Kahn tests were negative; the sugar content was 57 mg. per hundred cubic centimeters, and the total protein, 28 mg. There were no organisms on smear or culture. Roentgenograms showed a sclerosing process in the right mastoid.

Four days after admission there was definite tenderness over the mastoid. Radical mastoidectomy, performed by Dr. Frederick Stone, disclosed an acute process superimposed on an old chronic mastoiditis with destruction of the tegmen. There was a small cholesteatoma of the antrum and attic, and an epidural abscess was present in the middle fossa with localized pachymeningitis externa. The lateral sinus was normal. The squama was then removed until normal dura came into view. No fistulous tract was identified.

On the following day the patient was still drowsy and complained of frontotemporal headache, but there was less nuchal rigidity. The pulse rate varied from 50 to 86 per minute; the temperature ranged from 99 to 100 F. Within the next few days the headache subsided, but there was definite papilledema on the right.

On the sixth postoperative day the patient became excitable and could not be restrained; he insisted on leaving the hospital against advice. He returned six days later. During the interval he had had nocturnal headaches and was extremely restless. He vomited forcefully for two days before readmission. On the morning of entry he became drowsy; by afternoon he was stuporous, and that evening he was comatose.

The positive neurologic findings at this time were: rigidity of the neck; dilatation of pupils, the right being larger than the left, and poor reaction to light; facial weakness on the left side; flaccid hemiplegia on the left; absence of abdominal reflexes; bilateral Babinski and Kernig signs and ankle clonus on the right. The spinal fluid was clear and contained only 10 cells; there were no organisms on smear or culture. The temperature was 99 F., the pulse rate 75, and the respiratory rate, 15 per minute.

An operation was performed that night. An incision, 6 inches (15.2 cm.) long, was made from the mastoidectomy wound in an upward and medial direction, exposing an area of bone about the size of a half-dollar. Healthy dura was seen; the edges were coagulated with the Bovie machine. A ventricle needle was inserted into the temporal lobe, and at a depth of 3 cm. pus was obtained. The stylet was replaced, and a core of dura, brain and wall of the abscess was removed with the Bovie scalpel, and the Mosher basket was inserted. The patient almost instantly regained consciousness and began to move the left arm and leg. No organisms could be identified on smear or culture. The postoperative course was uneventful; the drain was extruded on the fourteenth postoperative day. The patient was discharged on September 9, having been out of bed for two weeks. Examination disclosed no abnormal signs. For over six months he has been working forty hours a week and has been without symptoms. The time which elapsed from the onset of the headaches to the day of operation was forty-five days.

Case 2.—A housewife, aged 32, who was admitted to the Brooklyn Jewish Hospital on Sept. 11, 1933, since an attack of scarlet fever and diphtheria at 4 years of age had had a chronic discharge from both ears with bilateral progressive deafness. The latter led to retardation at school and some lagging of speech. Though she could hear when spoken to loudly, she understood best by lip reading.

The patient had seemed well until three weeks before admission, when a profuse discharge was noted from both ears. Two weeks later she began to have pain in the left ear. Her physician found a furuncle in the left auditory canal, which he treated conservatively. Within the next two days pain recurred in the left ear, and the temperature rose to from 101 to 102 F. Two days before admission she began to have left-sided headache radiating to the occipital region. The temperature rose to 104 F., and she vomited once on the night before admission.

At the time of entry the patient appeared acutely ill and rather stuporous. There was a slight foul-smelling discharge from the left ear, and the canal was half filled with granulations. On the right were some granulations protruding from an old perforation in the drum. There was tenderness over the left mastoid. The pharynx and tonsils were injected. The temperature was 103.8 F., and the pulse rate, 110. The leukocyte count was 27,000, with 96 per cent neutrophils. There was marked nuchal rigidity, with bilateral Kernig sign and underactive reflexes. The ocular fundi were normal. Roentgenograms of both mastoids showed them to be markedly sclerosed, but on the left there was a punched-out area overlying the anterior wall of the sinus which was interpreted as possibly a chronic abscess or cholesteatoma.

The spinal fluid contained 5,800 cells, with 99 per cent neutrophils; the sugar content was 41 mg., and the total protein, 52 mg. per hundred cubic centimeters. Twenty cubic centimeters of antimeningococcus serum was given intravenously, and an equal quantity intraspinally. Smear and culture showed no organisms.

A radical left mastoidectomy was performed by Dr. Frederick Stone. A large cholesteatoma was removed from the antrum and the middle ear. The middle fossa was exposed, and normal dura was reached. A localized area of purulent exudate was found on the dura in the region above the antrum. On culture,

Staphylococcus aureus was reported. Part of the squama and the entire tegmen were removed. The lateral sinus was exposed and found to be normal.

On the following day the patient was more alert; the temperature was not as high, and the neck was less rigid. She improved steadily for about six days and then became restless and more apathetic. The neck was stiff, and the Kernig sign was positive on the left. The ocular fundi were normal. The spinal fluid at this time contained 2,600 cells, all polymorphonuclear; the sugar content was 50 mg. per hundred cubic centimeters; there were no organisms on smear or culture. One week following the mastoidectomy a serum rash developed, with fever, drowsiness, stiffness of the neck, facial weakness on the right side and hemiparesis and hemihypesthesia on the right with overactive reflexes on that side; in addition, the patient was somewhat aphasic. The condition improved within the text two days. The fundi were normal. Gross tests showed homonymous hemianopia on the right side. The aphasia and hemiparesis became worse; the abdominal reflexes could not be elicited; the Oppenheim response was positive on the right, but there was no Babinski sign. The patient gradually became more drowsy. The spinal fluid at this time showed only 110 cells, with 85 per cent lymphocytes. The smears and culture showed no organisms. On September 22, Dr. Ira Cohen and I carried out a procedure similar to that described in case 1, except that the defect in the bone was placed more anteriorly.

For the next three or four days the condition was no better, but there was no further discharge from the drain. Apparently the abscess had completely emptied itself. It was thought best to remove the basket and allow the exposed brain to herniate. Within the next two days the patient was more alert, though still aphasic and hemiplegic. On the sixth postoperative day she began to speak and move the right leg. She steadily improved in all respects, but on the twenty-third postoperative day papilledema of 2 diopters was noted on the left and beginning papilledema on the right. In the following two days papilledema advanced on the left, showing minute hemorrhages and exudate, and the right disk became completely obscured. These findings made us think of two conditions: either recurrent abscess of the brain or localized basilar leptomeningitis. The wound and clinical condition were progressing so favorably that we were inclined to favor a diagnosis of the more benign lesion. There was no change in either fundus for the following three days, and then both began to recede with the aid of magnesium sulphate administered by mouth.

The patient was discharged on October 25, thirty-three days after operation, at which time the fundi were normal; speech was practically the same as before operation, and there were no motor, sensory or reflex abnormalities. She has remained well since, though at times she has complained of inability to see things to the right. This has improved greatly; she has learned to accommodate herself to the defect in the visual fields so that she is no longer conscious of it. The visual fields show a right homonymous upper quadrantic defect. The time from the onset of the headache to the day of operation was eleven days. It is said that her hearing and speech at present are about the same as before operation.

DISCUSSION

Dr. Joseph E. J. King (by invitation): It makes little difference what method is used for the operation provided good results are obtained. In 1925, Cahill, who works with Mosher, presented some splendid results from the use of the British Army drain popularized in this country by Mosher. He described the procedure and the use of the drain. He stated that he incised the dura by making a crucial or three-limbed incision and then explored the area of underlying brain with a grooved director or Cushing needle. If he found an abscess, the drain with its plunger was guided along the grooved director into the abscess cavity without removing the director. The director and plunger were then removed. He made no mention of decortication or removal of any of the wall of the abscess. After the drain was in position in the abscess cavity, he fixed it to the dura and the scalp so as to anchor the drain in position. His intention was to have no dis-

placement of the drain, and there was no desire for herniation. The procedure used by Dr. Kaplan in his cases is based on the principles described by me, differing only in that he used the Mosher drain to encourage herniation of the abscess cavity. I have talked with Dr. Cahill since he wrote his paper, and he told me that in most of his cases there was a moderate degree of herniation after removal of the drain; i. e., there was a nubbin-like protrusion similar to a small mushroom at the site of the removal of the drain. It is my belief that the abscess cavity shrank about the drain like a deflated balloon and extruded itself as a small hernia, which granulated over and became epitheliated. This conception of what took place, therefore, differs somewhat from the illustrations in Cahill's original reprint, which show the remains of the abscess cavity as a fistulous tract.

I shall show a number of slides to illustrate the dangers of drainage according to the old methods of using a tube. If a drain is to be used, I consider that the Mosher drain is the best. All postotitic abscesses adjacent to the mastoid area, after becoming well encapsulated, are egg-shaped in the beginning with the small end directed toward the mastoid or petrous region. This portion of the capsule is much more fibrosed than the more distant portion and lends itself to the insertion and fixation of the Mosher drain. This portion is also frequently attached or adherent to the dura.

All who have treated abscess of the brain in the past have had disasters with the use of the stiff drainage tube. The first slide shows a tube placed in the abscess cavity. As the cavity collapses incompletely about the tube a secondary abscess is formed, and such an abscess is as dangerous as the original one. The next slide shows a tube fixed in position, and as the abscess cavity collapses and the ventricles dilate the further end of the tube is forced into the ventricle, resulting in meningitis and death. The next slide illustrates a tube which became displaced; in an attempt by an assistant to return the tube to its original position in its track the tube was pushed into the brain tissue itself and not into the original track. This produced a fatal result. The next slide shows a small soft catheter in the position described by Coleman. I have talked with Coleman about this procedure. It is my belief that in every instance in which the small catheter is used and kept in position for a long time a hard, firm track forms alongside the tube, and that after the small tube or catheter is removed this track remains and to all intents and purposes is a potential abscess which may later flare up and reform, especially if trauma is sustained. The next slide shows a section of a brain with such a track which formed following the use of a drainage tube. The brain was removed from a patient who was operated on at the Army General Hospital at Fox Hills on Staten Island in 1919. A drainage tube was in position for a long time. It was slowly shortened and finally removed, and the patient recovered. The abscess was in the right frontal lobe. The patient was intelligent and an instructor in aeroplane mechanics. One evening he was slightly unruly after drinking wine and was tapped on the head by a mounted policeman and brought back to the barracks. The next morning at about 10, he had a severe pain in the head while playing cards, seized his head with both hands and fell back unconscious. During the day a lumbar puncture was made, and the cerebrospinal fluid was extremely cloudy. The patient died about thirty-six hours after the head injury. One can see the thick-walled sinus which represents the remains of the abscess of the brain. The wall was about ¼ inch (0.6 cm.) in thickness and was practically avascular. It was somewhat similar to the thickened wall of a chronic empyema. The small cavity between the walls contained a thickened, brownish, inspissated material which had the appearance and consistency of peanut butter. The cause of death was rupture into the ventricle of this old abscess cavity, following trauma to the head, with the production of meningitis. The slides explain some reasons why I have given up the use of drainage tubes in cerebral abscesses.

In 1920, I operated in a case of temporosphenoid abscess, following which an accidental herniation of the abscess cavity took place. The cavity turned inside out and after treatment of the hernia with surgical solution of chlorinated soda

(Dakin's solution) the patient recovered. A short while later I operated in two other cases of abscess of the brain, one of the temporosphenoid region and one of the frontal lobe. In one case the tube became displaced, and in an attempt to reinsert it an assistant pushed the tube into brain tissue, and the patient died. In the other case the drain was removed after about two months and was followed by a recurrence of the original symptoms. It was reinserted in the abscess cavity, and the patient again improved. After a time it was again removed by an assistant, and symptoms of abscess of the brain reappeared. The patient died after a third attempt to reinsert the drain.

Since 1920, I have used the procedure which I reported in a paper read in Boston in 1924 (*Surg., Gynec. & Obst.* **39**:554, 1924). The intention is to make a fairly large opening directly over the abscess followed by a somewhat smaller opening in the dura after the dura has been fixed to the cortex with the coagulating electrode of the electrosurgical unit. This seals off the subdural and subarachnoid spaces and prevents meningitis. The cortex overlying the capsule of the abscess is then removed, the electrosurgical unit being employed. The presenting portion of the capsule of the abscess is removed; the abscess cavity is evacuated, washed out and inspected. No digital examination of the abscess cavity is made. The cavity is then allowed to herniate through the opening in the brain, dura and skull until it reaches the surface of the wound, i. e., until the cavity has become completely everted, and forms the surface of the dome of the hernia. This usually occurs between the second and the sixth day. By the use of this principle, death from the three common causes, meningitis, compression and rupture into the ventricle, is prevented. Formation of secondary pockets is likewise averted. In the past, it is my belief that I have allowed herniation to proceed to a greater extent than was necessary. Now, as soon as eversion of the abscess cavity has become complete, further herniation is prevented by lumbar punctures. The period of recovery is thereby shortened. I have had 11 cases in which recovery followed the use of this method and a twelfth case in which the patient is well on the way to recovery. Three patients who should have recovered, so far as the isolated abscess itself is concerned, died. One woman, who was operated on in Brooklyn and whose after-care was not supervised by me, tore off the dressing, stuck her fingers into the hernia and reinfected it. Until this time, herniation of the abscess cavity had taken place as it should. A few days after she removed the dressing and infected the cerebral hernia she died of meningitis. A girl at Bellevue Hospital was operated on for an encapsulated abscess of the frontal lobe after an operation had been performed for suppurative frontal sinusitis and the wound had healed. The abscess cavity herniated, and the patient was doing well when the infection of the frontal sinus flared up. Another abscess, which was not a secondary pocket from the original one, developed in the basilar portion of the lobe, and the patient died of rupture of this abscess into the ventricle without its being recognized. The third patient was a woman operated on at the Manhattan Eye, Ear and Throat Hospital for a well encapsulated abscess in the left temporosphenoid lobe. At the time of operation, however, she had pneumonia with a temperature of 104 F.; she died of pneumonia a few days after the operation. Other patients have died, but they had multiple abscesses or abscesses associated with leptomeningitis or acute suppurative encephalitis in which the capsule had not yet been formed.

Probably my most interesting case was that of a surgeon who was brought to the Manhattan Eye, Ear and Throat Hospital by Dr. Wortis last fall. The patient had had a severe infection of the lungs followed by an abscess of the right lung. On Sunday morning before admission he was able to drive his car. That night he was unconscious, and by Monday morning he was "out of his head," with a temperature of 104 F. This condition persisted until the following Thursday, when the temperature fell and he was mentally clearer. By Friday afternoon the temperature was 102 F., and he was sufficiently conscious to understand what was said, but he was unable to speak. A diagnosis of a metastatic abscess of the left cerebral hemisphere was made by Dr. Kennedy and Dr. Wortis. The pathologic condition was considered to be suppurative encephalitis or an abscess in its incipiency. The patient had complete hemiplegia on the right side, complete

hypesthesia on the right, amounting practically to hemianesthesia, homonymous hemianopia on the right and aphasia. On account of the wide area involved, Dr. Kennedy did not consider it advisable to wait for encapsulation but advised that I should operate. I knew that encapsulation could not have taken place between Sunday morning and Friday afternoon. I made a small trephine opening over the left parietal region and met no resistance with the exploring cannula. Some material, however, extruded itself alongside the cannula after the opening in the cortex was slightly enlarged. This appeared to be broken-down brain tissue. Because of experience in another case, I enlarged the opening in the parietal bone in a circular manner to a diameter of about 2 inches (5 cm.). The dura was excised, after being fixed to the cortex, so that the opening in the dura was somewhat smaller than that in the bone. The underlying cortex was somewhat softer than normal and was removed by suction. After removal of the cortex, broken-down necrotic brain tissue was encountered, some of which had the appearance of thick, yellow pus. This was removed by suction, and the affected brain substance was removed in all directions by suction until a cavity or excavation of considerable size resulted. This cavity was somewhat the shape of a thick-set ink bottle, larger below and smaller near the opening in the dura. All of the yellowish-looking affected brain tissue was not removed for fear of entering the ventricle. The excavation in the brain which remained following removal of the débris and detritus by suction was slightly packed with fluffed iodoform gauze and a copious gauze dressing soaked in surgical solution of chlorinated soda was applied. The iodoform gauze packing was slowly extruded and removed partly on successive days until the tenth day, when all of it was removed. By this time the portion of the brain substance which formed the floor of the excavation was on a level with the scalp. Although at the time of the operation this portion of the brain tissue had the appearance of being diseased, it now had a healthy appearance. The patient made a good recovery, and the wound was healed on about the forty-second day. The patient had completely recovered the use of the right leg, and the paralysis of the face had disappeared. He could make all motions with the right upper extremity, but these motions were weak. He had loss of position sense and astereognosis in the right hand. During his stay in the hospital he likewise recovered from the abscess of the lung. This case is reported in brief, and the method of procedure is offered for cases of massive suppurative encephalitis in which it is believed that the patient may not live long enough for encapsulation of the area to take place, or in which the area involved is so large that too much destruction of brain tissue would ensue if one waited for complete encapsulation.

Dr. Leo Davidoff: I am inclined to think that perhaps the Mosher drain has outlived its usefulness. Mosher, in his original paper, described the drain after having used it in only 3 cases, the results of which he did not record. He said that the reason for inventing the drain was that the rubber tube drains would not stay in place. He believed that his drain would. If anything, it would hold "too well." Since then it has been learned that by splitting the protruding end of a rubber tube and sewing it to the scalp the tube can be held in place and at the same time not so tightly that it will do what Dr. King demonstrated, namely, force its way into the ventricle when the abscess cavity shrinks. Recovery from abscess of the brain is still an unusual occurrence, and any method which will result in recovery is worth trying.

Dr. William D. Sherwood: Abscess of the brain is a most serious condition; having made the diagnosis one is faced with the question of proper treatment. This I do not think means so much the type of operation or the kind of drain as it does whether to operate at once or to postpone intervention for a number of days or weeks. Dr. King, I think, "hit the nail on the head" when he said the method of treatment, meaning the type of drain, was not important, provided the patient gets well.

To begin with, all abscesses of the brain fall into two groups. One group is composed of those abscesses which are the result of infected emboli from distant parts of the body, especially the lungs. These are apt to be multiple, and the

brain tissue suffers a terrific insult and is not always able to react with the formation of a capsule before it is overwhelmed by the severity of the infection. Usually one is forced to operate because of rapidly falling pulse and respiratory rates; no matter what the type of drain used, the results are uniformly fatal. The second group of abscesses are due to direct extension from the ear or the nasal accessory sinuses. These form slowly and are usually of low virulence, and often the track of the infection and the abscess itself are completely walled off. Here one may, without too much optimism, hope for a favorable result. I have seen excellent results following treatment of such an abscess in the frontal lobe of a child by Dr. Dandy's method of aspiration.

Too much emphasis cannot be laid on early diagnosis. One should not have to wait for hemiparesis before realizing that there is an abscess of the brain. A slight increase in one biceps or patellar reflex, an abdominal reflex moderately reduced and possibly a little less active plantar flexion should, taken with a suggestive history, make one aware of the possibility of an abscess. In the absence of urgent symptoms of pressure one can keep the patient under close observation and await encapsulation and more positive neurologic signs.

DR. IRA COHEN: No method is out of date that gives results such as Dr. Kaplan has shown this evening. Good results have been obtained with tubes, but there is no one method of drainage in cases of abscess of the brain which can be set aside as superior to all others, which is just what Dr. Frazier said in his editorial: How Shall We Treat Brain Abscess? (*Surg. Gynec. & Obst.* **57**:122, 1933). I believe that as the habits of abscesses of the brain (not the metastatic ones, but those due to extension) become more familiar the best mode of approach may be realized. With Bovie's electrocoagulation there has been improvement in results, but regardless of whether a tube or a Mosher drain or even simple aspiration is used, one must still keep an open mind and perhaps vary the method with various types of abscesses. Tubes are used so commonly throughout the country in well established neurosurgical clinics that one must accept the results they show. In Boston, I understand that the original operation using the Mosher drain, as Dr. King and Dr. Davidoff mentioned, has been replaced in most clinics by an operation such as was described by Dr. Kaplan. Good results are being obtained with this method.

DR. ABRAHAM KAPLAN: In the final analysis I suppose the surgeon is going to use that method which he finds most successful. There is no unanimity of opinion as to what is the best method. As to the time of operation, I wish to recall the presentation made before this society two years ago by Dr. Francis Grant, in which he reviewed 51 verified cases of abscess of the brain. In 39 of these, or 75.6 per cent, the abscess was correctly localized; in 19 the abscess was acute, a condition which has been termed "cerebritis." Not one of the patients recovered. Apparently drainage was instituted in these cases before the six week period. All the patients operated on six weeks or more after the onset of symptoms had encapsulated abscesses of one sort or another. Of the 30 patients with encapsulated abscesses, 20 recovered, and Dr. Grant's view, which I believe cannot be too strongly emphasized, is that few patients with abscess of the brain require emergency operation; the longer one waits the better the chance of recovery.

MULTIPLE SCLEROSIS: BRIEF PRESENTATIONS OF PATIENTS GIVEN QUININE THERAPY. DR. RICHARD M. BRICKNER.

A presentation of 10 cases is made in illustration of the type of improvements and remissions made by patients with multiple sclerosis who are being given quinine therapy.

DISCUSSION

DR. GEORGE H. HYSLOP: The theory behind the use of quinine is quite apart from the results of its use; the theory cannot be either proved or disproved by the therapeutic results. I have considerable respect for the hypothesis on which Dr. Brickner has been working. One must realize that the disease, which has been

an etiologic as well as a therapeutic problem for a good many decades, is going to remain a puzzle for at least another decade.

Dr. Brickner presented 10 cases this evening. Four or five years ago Dr. Osnato presented a series of cases in which the use of silver arsphenamine had led to what Dr. Osnato regarded as a more or less permanent state of remission. Spherula insularis vaccine was regarded as producing remissions. An interesting phenomenon of some significance was reported in conjunction with the use of Spherula insularis vaccine, namely, the production of a positive Wassermann reaction following its use. Of course, the production of a positive Wassermann reaction may have no bearing either on the cause or the nature of multiple sclerosis or on the therapeutic result, but the administration of the vaccine seemed to cause the reaction in patients to whom it was administered who previously had shown no evidence of spirochetal infection.

Dr. Brickner has been perfecting a technic of estimating the quantity of lipolytic substances in the blood of patients who have disseminated sclerosis. He is using as a therapeutic measure a substance which is presumed to have an antilipolytic action.

The statistical evaluation and the disappearance or improvement of certain symptoms or signs in a disease which is notoriously variable in its course are of small importance. Dr. Brickner should determine whether or not in patients who have been given quinine for an extended period of time the reaction of the blood shows any quantitative differences; then he can safely attribute any results obtained to the prolonged use of the quinine itself.

I have studied a few cases, but a small series proves nothing. Of 4 patients with acute cases, 1 could not tolerate the drug, and 2 were not followed long enough to permit the formation of any opinion. In the case of the fourth patient the disease was characterized by frequent exacerbations over a period of six years; while under my observation this patient had four episodes in one year from which she promptly recovered. She is a trained nurse and is working steadily now.

Of 4 patients with chronic cases, 1 seemed to be materially helped. One has a mild form of the disease, in that though it has been present for fourteen years he is able to work; and he has taken quinine for the last two years, during which period the disease has been stationary. Another patient who has had the disease for eighteen years is doing office work and has had four episodes which improved with the use of quinine. The other 2 patients showed no response.

One must be careful in attributing results to the use of any particular measure unless there is a control series of cases that are similarly grouped as to the type of the disease. That means a large series of patients in each group, perhaps 100 without any treatment, 100 given quinine therapy, 100 given foreign proteins and 100 given some other kind of therapy. Unless such control series are used, from the standpoint of judging treatment one really does not accomplish anything. The cooperation of neurologists is necessary. I urge that Dr. Brickner's work be continued and that he check his therapeutic results with control measurements of the reaction of the blood, which I understand have some diagnostic value in the case of persons who are in the acute phase of the disease.

Dr. Gerald C. Parker: At the Long Island College Hospital, under the supervision of Dr. Perkins, my associates and I have had a series of cases of multiple sclerosis in which the patients have received quinine therapy, and the results have been somewhat gratifying. There have been some rather startling remissions, while some patients have not shown as much improvement as was hoped for. I cannot agree with Dr. Brickner on what he calls a remission. I would call some of these patients slightly improved rather than say that they are having a remission, because some of them still seem to show considerable evidence of the disease.

We have had a few patients who could not take quinine readily at first, and we have reduced the number of doses a day rather than the size of the dose; in this way we have been able to return to the usual 5 grains (0.32 Gm.) three times a day. I believe that quinine really offers some hope in the treatment of multiple

sclerosis; this is borne out by Dr. Brickner's series and our own, which amount to some 20 cases.

DR. LEON H. CORNWALL: I wish to suggest that such studies as these should be controlled by the observation of an equally large group of patients who are not given therapy.

DR. BERNARD SACHS: Dr. Brickner said that he was not drawing any conclusions from his cases; it is particularly difficult to evaluate the merits of any therapeutic agent in a disease that is subject to remissions and exacerbations, as multiple sclerosis is. One can judge of the effect only in a large series of cases and over a long period. The quinine treatment is simple and can be continued for a long time; no elaborate apparatus is needed. I think that it will be wise to continue this treatment for a long time until a much larger series of cases is assembled.

I do not know whether the disease is becoming more frequent, whether the diagnosis is made more easily or whether a great many different conditions are being grouped under the title of disseminated sclerosis. In any study that is made, I think that a point which would be of far greater interest than the therapeutic results would be an intensive examination of the causes that led up to the disease, so that one might learn to what the disease is due.

DR. H. A. RILEY: I think that any one who demands that an individual physician collect a series of 400 cases of multiple sclerosis in one lifetime is asking for an impossibility; when any one suggests that a group of patients be observed who are not given any treatment, he is again making an impossible request, for no group of patients will remain faithful to a physician when he is not treating them. Many physicians are treating patients for multiple sclerosis with arsphenamine, hyperthermia, pills, massage, rest combined with medication and many other therapeutic means; these may serve as Dr. Brickner's controls. It is not essential for him to establish his own controls, and I think that it is necessary for him to treat every patient he can with quinine in order to build up as large a group as possible and to compare his results with the therapeutic effects obtained by other forms of treatment.

DR. HELEN ROGERS (by invitation): For three and a half years I have watched the work done with Spherula insularis in England; Purves-Stewart did not check his results with control studies. It seems to me that Dr. Brickner is the best one to check his own results. After all, how can various workers check each other's work? Dr. Hyslop's project is a big one—to collect 400 cases—but I think that it is the only solution to an evaluation of the therapeutic results in cases of multiple sclerosis; the sooner some one studies a series of 100 patients who are not receiving therapy, 100 who are receiving fever therapy, 100 who are receiving Spherula insularis vaccine and 100 who are receiving quinine, the quicker a conclusion will be reached.

DR. RICHARD M. BRICKNER: This presentation was made not alone for the sake of illustration, as I said at the beginning, but also to see whether some more uniform and perhaps active interest in the therapy of multiple sclerosis might be stirred up. No pretense has been made that quinine is the only, or even necessarily the best, treatment for multiple sclerosis. I have been extremely conservative in making any claims for it, being fully aware of what spontaneous remissions do. Nevertheless, detailed observation, which has been made over a fairly long period, has convinced me that the 49 patients studied have done well.

The question of controls has been difficult from the beginning, and still is. It would be splendid if it were possible to have different series of 100 patients, each treated in different ways, as Dr. Rogers suggests. In this country it does not seem possible for any one man to obtain enough patients to accomplish this. In the past five years I have been able to get together only a few more than 100 myself, and not all of them were available for treatment. For control purposes I have had to use the results of general experience and observation on those patients I have had myself who were unable to take quinine. It would have been

impossible for me to build up a series of patients given quinine therapy unless, as Dr. Riley has indicated, I treated every patient I could with quinine.

I agree fully that the whole question of quinine therapy will never be given a scientific orientation until several extensive control series can be intensively studied. Personally I should be glad to collaborate with any one who wishes to institute some other form of therapy, analyze it and compare the results obtained with those obtained with quinine. Perhaps a group could be formed to study the therapy of multiple sclerosis, with different persons conducting the various types of therapy; one group of patients who did not receive therapy might be observed. If such a move were carried out it would be essential that all of the investigators apply the same standards of observation and analysis. At the present time Dr. Schick at the Neurological Institute has begun to analyze the records of all patients with multiple sclerosis under treatment other than quinine in an effort to establish a control series.

Dr. Sachs mentioned that this work should be continued. I expect to continue it, but what I should really like to see is its continuation by others. I believe that the results of any one who originates a treatment should be checked by some one else.

Dr. Hyslop spoke of acute and chronic cases. Of course the earliest ones are the best for treatment. Of his 4 early cases, only 1 was available for study for any period. One patient stopped treatment after six weeks; I have found that usually from four to six weeks elapse after treatment has been instituted before improvement commences.

I agree with Dr. Parker that the patients whom I presented do not all show remission. I should say that 6 have had remissions and that 4 have shown marked improvement.

ATYPICAL CASE OF SYNDROME OF TONIC PUPILS AND ABSENCE OF REFLEXES. DR. WALTER BROMBERG (by invitation).

In February 1932 a girl, aged 19, who had made a good adjustment, won friends easily and had an open type of personality was admitted to the Bellevue Hospital with a history that for about eight months she had been nervous, irritable and depressed; she also complained of loss of ability to concentrate. She had been keeping company with a young man for some time, and a quarrel with him had precipitated the depression about six months prior to admission. She had amenorrhea at that time. A week prior to entry she had been under treatment at another hospital on recommendation of a neurologist because of her mental state and pupillary irregularity. There she was depressed, refused to eat for two days, became very excited following a lumbar puncture and cried persistently; being unmanageable, she was transferred to the Bellevue Hospital.

In the hospital she complained constantly of pain following the lumbar puncture. She was moderately depressed; she said she was worried about not menstruating, could not concentrate or work and had no interest in anything. She worried about how her life would turn out. She said: "I worry about myself too much. I was melancholy."

Physical examination revealed a pyknic, slightly obese type of body build but no other significant somatic findings. The Wassermann reaction of the blood and spinal fluid was negative. The chief interest was in the pupils, which were unequal, the right being larger than the left; the right was ovoid in a vertical direction, and measured 4.5 mm. in the longest diameter; the left measured 3 mm. and was ovoid and slightly more irregular. Sometimes both pupils were wider, but unchanged in relative size. On repeated examinations the reaction to light (direct and consensual) on the left was at one time absent and again prompt but through a small arc; the right pupil usually reacted promptly through a small arc. The accommodation reaction was present in both eyes; it was prompt but not complete. The convergence reaction was the same. The left pupil, the smaller one, reacted less than the right to light and in accommodation and convergence. Pressure in the iliac region or strong muscular pressure did not change the pupillary

reaction significantly (Meyer and Redlich phenomena). There were no disturbances of the ocular muscles and no defects of the visual fields; the fundi showed medullated nerve fibers. No gross disturbances in vision were present. There was no change in sensation, in the cranial nerves or in cerebellar function. Motor power was good in all muscle groups. The reflexes were diminished in the upper extremities and not always elicitable. The knee jerks could not always be obtained; at times they were present; at times reinforcement was required. The ankle jerks were never obtained with repeated trials, even with reinforcement maneuvers.

There was no history of previous illness except an attack of diphtheria at the age of 2, which was promptly cured by antitoxin and from which the patient recovered uneventfully without sequelae. The family history did not reveal syphilis; the Wassermann reaction of members of the family was negative. The patient gave no history of trauma to the eye, retinitis, poliomyelitis or muscular dystrophy. She had never expressed subjective complaints about the eye. The mother had always noticed that the eyes were unequal; on a previous occasion the reaction of the blood of each member of the family had been examined to settle the question of congenital syphilis because of the patient's pupils.

The mother, aged 42, of typical pyknic constitution, was examined. The ankle and knee jerks were absent on several examinations, but on later examination, before a conference, the knee jerks were present and one ankle jerk was faint. A brother (J), aged 14 years, had a diminished ankle jerk on the right and a questionable ankle jerk on the left. In an older sister (A), aged 21, the ankle jerks were absent, but the knee jerks were present. In all other members of the family (the father was not examined) the pupils and fundi showed no disturbances; all claimed to be in good health.

The case was regarded at first as an example of familial loss of tendon reflexes with anomalous pupils, possibly congenital in origin. Later, attention was drawn to an article by Adie *(Brain* **55**:98, 1932), who described the syndrome of tonic pupils and absence of reflexes. He collected 60 cases, most of them from the ophthalmologic literature, and included 19 of his own. He spoke of it as a benign syndrome. Tonic pupils have been known since 1902 (Sanger and Strassburger). Other cases have been described, notably by Foster Moore, Axenfeld and Behr, and the condition has been given the names of nonsyphilitic Argyll Robertson pupil, pseudo-Argyll Robertson phenomenon, Marcus pupil phenomenon, pupillotonia, myotonic pupillary reaction, nonsyphilitic pupillary inaction, iridoplegia interna, etc. In some of these cases no neurologic examination was made, but many showed absence of ankle jerks. Adie concluded that these cases could be grouped together and that the characteristic form of the syndrome consisted of tonic pupils with absence of reflexes occurring in the absence of syphilis or other demonstrable disease of the nervous system. The tonicity of the pupil is always unilateral; the affected pupil is frequently ovoid, is most often dilated and has the following characteristic myotonic reactions: no, or practically no, reaction to light (direct or consensual) and an excessively slow reaction in accommodation and convergence. There is often misty vision owing to a slow accommodation reflex. In both reactions, after an initial retardation the pupil of the tonic eye contracts beyond the normal point of contraction for the other (normal) eye and after a period it slowly dilates (beyond the normal point of dilatation). This reaction is true for light also. The convergence reaction is the most typical one of the syndrome. Adie concluded that the picture is due to a perversion of pupillomotor activity and in some way is a manifestation of disorder of the vegetative nervous system. He considered the tonic movements as being qualitative changes in movement and not complete paralysis. Other cases which he described as incomplete forms may show only (1) tonic pupil, (2) absence of reflexes alone, (3) atypical phases of tonic pupil (iridoplegia), or a change from one phase to another, and (4) atypical phases of the entire picture.

In my case the outstanding finding, besides absence of reflexes, is the changing pupillary reactions—at times inactivity to light, and at times reaction occurring in the left eye (the smaller one) and to a slight extent on the right also. This is

not the myotonic pupillary reaction. These changing pupillary reactions are closer to those seen in cases of catatonic schizophrenia. This patient had a transient psychosis, best described as a mild depression, from which she recovered. There is no sign at the present time of any schizophrenic stigmas. The personality was typically syntonic. It is interesting that in a person with an abnormal affective reaction there should occur changes similar to those observed in catatonia.

These so-called catatonic changes, consisting of spontaneous periods of pupillary rigidity with changes in shape and size, were observed by Westphal in 1907 and by Bumke about the same time. Later, E. Meyer observed that pressure against the iliac point will bring about these changes and Redlich found that strong muscular exertion will accomplish the same thing. Pupillary rigidity has been seen occasionally in patients with alcoholic encephalopathia and at times in patients given paraldehyde or other medication.

The general formulation, then, is that in my case a constitutional structural anomaly of the vegetative and the somatic nervous system underlies the pupillary changes. Pupillary changes may occur: (1) under the influence of toxic factors interrupting the function of the vegetative nervous system; (2) under the influence of the emotional state, as in a psychosis, and (3) when there is a structural change or anomaly in the nervous system, along the efferent or afferent arcs of the pupillomotor fibers or in the center in the midbrain. This case is described best as an anomalous type of pupil in a person with abnormal reflexes not due to disease; it belongs in the last group. In this there may be some structural change in the nervous system which allows absence of reflexes and a peculiar pupillary reaction. The case suggests, therefore, that the group described by Adie may be much larger and include a greater variety of pupillary anomalies than he detailed.

DISCUSSION

DR. H. G. WOLFF: Probably the chief significance of the syndrome described by Dr. Bromberg rests in its recognition and differentiation from more malignant syndromes. The criteria he mentioned by which the pupil may be known are simple. However, the pathophysiology underlying the combination of unilateral pupillary defects and bilateral changes in the tendon reflexes is not easy to understand.

In addition to actual lesions in the reflex arc, even slight changes in the internal environment change simple reflexes. Thus, Graham Brown has shown that stepping in the hind limbs of a spinal animal is augmented by asphyxia. Rosett and Foerster pointed out that hyperventilation increased tendon reflexes and made reflex abnormalities in hemiplegic patients more apparent. Tourney observed that in patients with Cheyne-Stokes' breathing the extensor plantar response is more readily elicited in the apneic than in the hyperpneic phase. The effects of inducing contraction in neighboring muscles (as in so-called reinforcement) on the knee jerk and rebound or clonus phenomena are well known. Also the absence of pupil and tendon responses in patients who have just had generalized convulsions is familiar. In delirium from various causes, notably from bromide, the pupillary and tendon responses are occasionally sluggish or absent.

Moreover, certain chemical agents alter the simple reflexes. Thus, Altenburger and Kroll observed that the refractory period of the wink reflex elicited by blowing a gentle stream of air against the cornea was increased by the intravenous administration of epinephrine and calcium and depressed by choline, pilocarpine and potassium.

Rosenfeld, Elliot and Walsh noted that scopolamine made it easier to elicit the extensor plantar response in patients with functional impairment of the corticospinal system.

It should be emphasized that the autonomic nervous system, with the exception of the mechanism involving the pupillary response, does not seem to be peculiarly or especially involved in the syndrome under discussion, as far as I know. There is no good evidence that the stretch reflex is greatly altered by removal or stimulation of the autonomic fibers of the implicated muscles.

In mentioning a few of the many mechanisms that may alter simple reflex reactions, I do so, not with the desire to indicate that any of them is concerned in the pathogenesis of the syndrome described by Dr. Bromberg, but rather to indicate the multiplicity of factors that enter into the consideration of the interesting phenomena described by him. In no known single mechanism rests a satisfactory explanation for the described aberrant reflexes.

Dr. Paul Schilder: In the clinical material at the Bellevue Hospital nonsyphilitic pupillary disturbances have been observed in a great number of cases. In cases of acute alcoholic intoxication, complete rigidity of pupils is comparatively rare. Much more commonly the pupils are sluggish and show changing reactions, sometimes reacting, sometimes not. When the pupils react, they often become inactive when pressure is exerted on the sacro-iliac point or when a patient exerts muscular pressure himself. A similar disturbance can be observed after injections of scopolamine and morphine when the severe pupillary disturbance has disappeared. In catatonic patients similar pupillary reactions may be present. Whereas catatonic pupillary disturbances are comparatively rare in white persons, they are common in Negroes. Many years ago I observed severe pupillary disturbances in a catatonic white patient, whose normal sister showed pupillary disturbances of a similar type. Changing pupillary rigidity is therefore dependent not only on toxic factors but also on constitutional and racial peculiarities influencing the nervous system. It is of particular interest that in Dr. Bromberg's case the pupillary changes are connected with familial abnormalities in the ankle jerks. The case opens the way to a deeper understanding of the constitutional factor in pupillary disturbances.

Gestalt Function Visual Motor Patterns in Organic Disease of the Brain, Including Dementia Paralytica, Alcoholic Psychosis, Traumatic Psychoses and Acute Confusional States. Dr. Lauretta Bender (by invitation).

This article was published in full in the February issue of the Archives, p. 300.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, May 17, 1934

Albert W. Stearns, M.D., *Presiding*

Congenital Deaf-Mutism and Retinitis Pigmentosa Occurring in Siblings. Dr. Emeline P. Hayward.

Deaf-mutism has been classified (Fraser: *J. Laryng. & Otol.* **45**:538, 1932) as follows:

1. Constitutional or congenital.
   - (*a*) Sporadic.
     - (1) Michel's type—aplasia of the labyrinth.
     - (2) Mondini's or Alexander's type—malformation of the bony and membranous labyrinth. The organ of Corti may be absent.
     - (3) Malformations affecting both the cochlear and the vestibular apparatus associated with retinitis pigmentosa and mental enfeeblement.
     - (4) Scheile's type—saccular-cochlear malformation. Seventy per cent of congenital or developmental deaf-mutism is of this type; the vestibular apparatus reacts normally to rotation and caloric tests.
   - (*b*) Endemic or cretinic.

2. Inflammatory or acquired.
   (*a*) Traumatic—fracture of the base involving both labyrinths.
   (*b*) Congenital syphilitic—due to syphilitic meningitis with secondary neurolabyrinthitis or secondary to syphilitic otitis media breaking through the window.
   (*c*) Due to labyrinthitis following purulent meningitis.
   (*d*) Due to labyrinthitis following suppuration in the middle ear.

There are not many references in the literature to a combination of congenital deaf-mutism with retinitis pigmentosa in two members of one family. Fraser, of Edinburgh, described a form of congenital or constitutional deaf-mutism wherein the malformation affects both the cochlear and the vestibular apparatus. This is said to be associated with retinitis pigmentosa and mental enfeeblement. In these cases vestibular reactions are diminished or absent, and the gait is uncertain. The most marked changes are hypoplasia of the sensory epithelium in both parts of the membranous labyrinth, atrophy of the cochlear and vestibular ganglia, alterations in the blood vessels and changes in the brain.

The patient presented here is a Jewish woman, aged 29. The known family history on the father's side does not reveal any neurologic or mental disease or defect of the special sense organs. The maternal grandfather died at the age of 46 after two years of an illness characterized by slowly progressive paralysis of some sort. The maternal grandmother had generalized convulsons at the age of 55, and these continued until death at the age of 75. A maternal first cousin is a deaf-mute. The mother suffers from diabetes and hypertension. The patient is the fourth of four living children. There was one miscarriage. The first born, a man, aged 37, has the same physical handicaps as this patient; i. e., he has been deaf-mute all his life, has retinitis pigmentosa with marked impairment of vision and, when younger, had a staggering gait. He, like the patient, tends to emotional instability. His economic history as well as the impression gained at an interview with him speak against a mental enfeeblement of appreciable degree.

The patient was born in 1905 without unusual circumstances. As a baby she was considered weak and was retarded in learning to sit up and later to walk. She never learned to balance herself, walking with a definite stagger. There were no neurotic traits as a child. She entered the Horace Mann School for the Deaf at the age of 6 and was graduated at 15. She then spent two years at high school and three years at a trade school.

From the ages of 20 to 25 she held a position painting cards. At this time she became aware of spots before her eyes, dimness of vision and some diplopia. The condition was diagnosed as retinitis pigmentosa, and a cataract was removed from the right eye. The patient received roentgen treatment to the eyes, but vision became progressively worse. Cervical sympathectomy was performed on the left side, and the patient felt that vision became brighter, but it has changed little since that time (three years ago).

The patient was brought to the Boston Psychopathic Hospital on May 6, 1934, because of violent rages, usually provoked by contact with the brother whom she vaguely holds responsible for most of her difficulties. She has attacked him and her mother during these reactions. Following this disturbance she attempted suicide.

Physically, beyond the defect of the special sense organs and the scar due to the cervical sympathectomy, the patient presents no anomalies. She cannot distinguish objects with the right eye but does distinguish light. There are bilateral congenital cataracts, the right having been operated on. The fundus on this side is seen with a + 12 lens and shows the characteristic pigment. Vision in the left eye is 20/100. Examination of the fundus of this eye revealed pigment, more at the periphery. The visual field of the left eye showed a contraction to 5 degrees.

Otoscopic examination revealed an entirely normal external auditory canal and drum head on both sides.

The patient is deaf to all ordinary sounds. Tested with the audiometer, she heard middle C at maximum intensity with both ears. With the right ear she heard an octave below and with the left occasionally an octave above.

The patient staggers in walking. There is no spontaneous nystagmus or spontaneous past pointing. On rotation there is no nystagmus, past pointing or postrotatory vertigo. Caloric tests indicate that the semicircular canals are not entirely dead, as under certain circumstances a rotatory nystagmus is obtained. But the patient does not pastpoint at any time and, from the irregularity of the nystagmus it is evident that the canals are seriously impaired, the left horizontal more than the others.

The Muck test was negative. This test consists of rendering the nasal mucosa anterior to the inferior turbinates ischemic by means of epinephrine, and then marking a line parallel to the floor of the nose with a probe. If the reaction is negative, the line becomes hyperemic; if it is positive, the line becomes dead white and remains so longer than the surrounding area of ischemia. Karl Huber found the Muck test negative in cases of hereditary familial deaf-mutism except when some intercurrent disease that would alter the reaction had occurred (meningitis, encephalitis, scarlatina with otitis, tuberculosis, syphilis, disease of the middle ear or primary labyrinthitis). He recommended the use of the test for differentiating between familial deaf-mutism and that occurring at an early age. If this is reliable one may conclude that the deafness in this patient is of the hereditary familial type.

Wassermann tests of the blood and spinal fluid were negative.

Mental examination has revealed a woman of probably average intellectual capacity who is capable of making good rapport with those attending her. She is orderly and cooperates well in ward routine and in the testing. She is self-conscious and hypersensitive, preferring not to mingle with other patients. Her speech is characteristic of deaf-mutes; all interrogation and interviews are conducted in writing. The stream of thought tends to be diffuse. She appears cheerful superficially, but her writings indicate depression. She blames her brother for her inability to get along on the basis that he reminds her of her deafness. He has obstructed her marriage and prevents her from making friends. Most of this is of a misinterpretative nature. She is much preoccupied with the topic of marriage. She has had no hallucinatory experiences. Her judgment is poor, but her insight is fair.

TREATMENT OF HYDROCEPHALUS BY ENDOSCOPIC COAGULATION OF CHOROID PLEXUSES. DR. TRACY J. PUTNAM, Boston.

Transcortical resection of the choroid plexuses of the lateral ventricles has been the only operation so far reported which has produced permanent relief from pressure in any series of cases of communicating hydrocephalus. The operation, however, has a high immediate mortality and is apt to produce severe cortical damage as a result of retraction and collapse of the ventricular walls, so the end-results have not been wholly satisfactory.

A new instrument has been devised to carry out the aims of the operation while partially obviating its disadvantages. This consists of a rod of optical glass, 5 mm. in diameter and 15 cm. long, bearing a small light and two electrodes in grooves. It is introduced through a bur hole with a minimal loss of fluid or blood. Through it the various structures within the ventricle may be recognized and a large portion of the choroid coagulated. In the six cases in which it has been used the pressure has been relieved, the growth of the head has ceased and the thickness of the cortex has remained unaltered. There have been no deaths following the operation, and the reaction has been slight.

DISCUSSION

DR. J. B. AYER: I wish to ask Dr. Putnam if in these cases he carried out any studies on the spinal fluid pressure before and after operation; also if he carried out any dye tests. With regard to the technic, I can vouch for the fact that with his instrument one who is not trained can see well in the isolated brain, and it is reasonable that vision in the living brain would be even better. I hope Dr. Putnam has brought his instrument here for others to be convinced of this.

DR. F. FREMONT-SMITH: Is there any evidence as to the regeneration of the choroid plexus?

DR. G. HORRAX: It seems to me that this is an important communication. Dr. Putnam has been most ingenious. Many have struggled with little success in dealing with patients with hydrocephalus. Some of the children are perfectly intelligent. It seems to me that the ideal way of dealing with this type of case is not to let the fluid out of the ventricles. When the fluid is allowed to flow out it is a shocking operation, and while patients may recover they react badly. My co-workers and I have had great difficulty in holding the hemisphere out so that it does not sag away from the dura. I have often wondered how effective it would be if one had some instrument such as genito-urinary surgeons use and whether one would be able to see sufficiently through fluid which must get turbid from the heat, etc. In this approach, in the choice of site is it possible to coagulate practically the whole of the choroid on that side or does one have to look around corners, etc? The anterior part is pretty closely adherent to large veins, and I should think one might experience trouble.

DR. H. R. VIETS: The prevention and control of hydrocephalus after operation for spina bifida has always been a problem. I think that Dr. Putnam spoke of a case in which this operation had been done. If this was done first would it allow a successful operation on the spina bifida? If this is a way that hydrocephalus can be prevented, it is an important part of the whole picture.

DR. D. MUNRO: I wish to add my word of praise. Dr. Putnam's method is a great step in advance, and while he has given only a preliminary report it calls for congratulation.

DR. W. J. MIXTER: I have been much interested in watching this method develop. Dr. Putnam has done an interesting piece of work. I think I can answer Dr. Horrax's question as to whether the ordinary cystoscope can be used in the ventricle. I tried to cure hydrocephalus by breaking through the floor of the third ventricle. It worked in only one case. It is hard to see in the ventricle with the ordinary cystoscope, especially when the spinal fluid becomes a little bloody. One cannot wash the ventricle out and get a clear medium, as in the bladder.

DR. P. YAKOVLEV: Dr. Putnam did this operation in a case at Monson State Hospital, and the child is doing well.

DR. TRACY J. PUTNAM: I have attempted to study the spinal fluid pressure, but in infants this can be done satisfactorily only at the time of operation with the patient under the influence of a nonvolatile anesthetic. In cases in which I have measured the pressure under avertin anesthesia it has varied from 200 to 300 mm. at the time of the first operation. It is usually possible to demonstrate a decrease in pressure at the time of the second operation, and this is demonstrated also by a collapse of the fontanel. Phenolsulphonphthalein has been used in a few cases, and the pressure has always been found to be reduced, but it has not seemed to help in deciding whether or not operation should be performed.

I have no real information about the regeneration of the choroid. The choroid has been found to be atrophied in extreme cases of hydrocephalus, and this might be taken as evidence that it does not regenerate. It did not regenerate in Dandy's experimental animals, and I know of a few patients who have been cured for a matter of years by open resection of the choroid. I believe that the present instrument is far better than the common cystoscope or urethroscope because in the latter instruments there is a complicated lens system which absorbs a great deal of light and they can operate only at a fixed focus. I believe that an important advantage of my instrument is that it carries both electrodes, so that the heating current does not run through brain tissue. Only the choroids in the lateral ventricles can be reached by this procedure, but they constitute at least 80 per cent of the whole bulk of the plexus.

MOTION PICTURES IN COLOR OF THE FIRST SIX CRANIAL NERVES. DR. P. E. TRUESDALE, Fall River, Mass. (by invitation).

Book Reviews

To Be or Not To Be: A Study of Suicide. By Louis I. Dublin, Ph.D., and Bessie Bunzel, M.A. (of the Metropolitan Life Insurance Company). Price, 3.50. Pp. 443. New York: Harrison Smith & Robert Haas, 1933.

A careful study of the problem of suicide would be a great contribution to society at any time but is particularly worth while at a time when there is great stress and strain on social life in general. This book is based on a careful and thorough study by two statisticians of the staff of the Metropolitan Life Insurance Company. Information regarding the situation is, of course, of definite economic significance to insurance companies and at the same time becomes a contribution to a greater understanding of all the factors relating to suicide in general.

The first sections of the book deal with general problems, such as the prevalence of suicide, the influence of environment, the historical background and the aspects as regards law and life insurance. The latter sections take up the psychologic aspects and what relation suicide has to mental disorders and, finally, what may be done in the prevention of suicide. The authors show that they have consulted many sources of information, as well as the statistical statements that have been available in the files of insurance companies. They show an acquaintance with much psychiatric and psychoanalytic literature and cite various authors and contributors, most of whom have written from the psychiatric point of view. Probably that is because their study has shown that the deeper aspects of suicide are more important than the ordinary sociologic considerations that are so often given great significance.

The following isolated sentences or statements show the trend of some of the contents of the book:

"It seems far more probable that natural and racial proclivities toward suicide are readily modified by the environment and are the result of social rather than of biological heritage . . during the years 1926 to 1930 the four methods used by 84 per cent of all the suicides were in order of frequency—shooting, hanging, poisoning, and asphyxiation. . . High suicide mortality among physicians and dentists probably results in part from constant occupational contact with convenient means of suicide. . . Suicide predominates at both ends of the social and financial scale although chiefly at the upper end. . . On the whole in primitive communities the women rather than the men more frequently commit suicide." The last statement is not in keeping with the findings of the study as a whole, for the incidence of suicide is much higher in males than in females in civilized communities.

In various sections several interesting points are brought out: that suicide has a high incidence in single persons, in urban rather than in rural communities, in the Teutonic race and in the western part of the United States and is more frequent in spring and summer than in other seasons. The incidence is low in Catholics, Latins, Negroes and the southern part of the United States. "When the rate remains moderate suicide must not be regarded as a morbid phenomenon. . . . Only when the rate becomes excessive is there an indication of an unwholesome social state." This statement explains perhaps why the rate among the Jews in Germany has become unusually high in recent years, although the study shows that ordinarily the rate is low in the Jewish race. Other significant statements are:

"Although material conditions in group patterns are inhibiting or encouraging forces, suicide is after all always a personal reaction. . . The external factors we have been examining in the preceding chapters of this book are the secondary causes; the primary causes of suicide lie hidden in the depths of the human personality . . . very frequently homosexuality is found to be behind suicidal impulses. . . Both underweights and over-weights show excessive mortality in suicide . . . if in addition to making economic life somewhat more secure we can likewise help individuals to straighten out the intimate personal problems that

are tormenting them beyond endurance, we shall have made real progress in our attack upon suicide."

An interesting discussion on communism in Russia is given, the authors pointing out that if communism can be regarded as a religion like other religions it has exerted an influence on suicide in that there does not seem to be a large problem of suicide in Russia at present, in spite of real physical want and hardship.

The book as a whole contains much more of interest than one would ordinarily find in a statistical study of this nature. There is perhaps a little too much psychoanalytic theory expounded in connection with the reasons which lie behind attempts at suicide. This, however, is understandable if it is remembered that the psychiatric, and particularly the psychoanalytic, field has made great contributions to the understanding of the deeper fundamentals in human reactions.

In the appendixes a number of valuable tables are given that make the reading of the book much more exact and enjoyable. In addition, there is a good bibliography that should be valuable to workers interested in this subject.

L'olive bulbaire. By P. Mareschal. Price, 40 francs. Pp. 217, with 44 illustrations. Paris: Gaston Doin et Cie, 1934.

This monograph on the inferior olive deals with a subject which is greatly in need of clarification. The first part of the book is given over to a review of the anatomy of the olive; its connections with the cerebellum, mesencephalon, diencephalon and spinal cord, and its blood supply, histology and ontogenesis. In the second part a study of the phylogenesis of the olive is taken up, this portion consisting of original work by the author. These studies were made chiefly on monkeys and anthropoid apes. Finally, a brief consideration is given to the hypothecated functions of the olive as a coordinator of movements of articulation, as a center of vertical posture, in rigidity and in velopalatolaryngopharyngeal clonus.

Mareschal comes to the following conclusions: Anatomically, the olivary complex is connected with the cerebellum by crossed olivifugal tracts passing through the inferior cerebellar peduncle and terminating in the dentate nucleus and cerebellar cortex for the principal olive, in the superior vermis for the dorsal accessory olive and in the inferior vermis and paraflocculus for the internal accessory olive. The olivary complex is connected with the spinal cord by the tract of Helweg, which is chiefly descending. It is connected with the mesencephalodiencephalic areas by the central tegmental tract, a descending olivipetal tract from the thalamus, red nucleus and corpus striatum. Anatomic studies indicate that the olive is a part of a vast system of subcortical sensorimotor integration.

Phylogenetic studies show that the bulbar olive is formed first by the internal parolive (chicks) and then by the dorsal parolive and the principal olive (birds). The principal olive is at first only a small formation in the concavity of a dorsomedial arc formed by the union of the dorsal and internal parolives (Echidua). The enormous development of the olives in mammals proceeds from this arc. The internal parolive is the oldest part of the complex. The dorsal parolive, on the other hand, is a recessive organ and tends to disappear in the anthropoid apes. The development of the principal olive occurs chiefly at the expense of the dorsal leaf, mostly in a caudal and lateral direction.

The portion of the monograph dealing with the phylogenesis of the inferior olive is well done. The monograph represents a useful compilation of knowledge concerning the olive and can be recommended highly.

Heredity and Environment; Studies in the Genesis of Psychological Characteristics. By Gladys C. Schwesinger. Edited by Frederick Osborn. Price, $4. Pp. 484, with 33 illustrations. New York: The Macmillan Company, 1933.

Schwesinger and Osborn believe that methods of measuring psychologic characteristics have been worked out sufficiently to make possible objective scientific research on the problem of heredity and environment, and that with constantly

improving technics a solid body of knowledge on the subject will soon be achieved. They have therefore prepared an outline of the present knowledge on this subject and a reference book for future work. It is an excellent summary of the present status of the problem.

The first sections describe the tests by which intelligence and personality traits may be estimated and represent a timely survey not only for the student of eugenics but for all psychologists or psychiatrists who face the practical problems of judging intelligence and personality characteristics. It need hardly be noted here that studies of intelligence are more fully developed than studies of personality. In the chapter "Measurement of Personality" Schwesinger points out the many important problems which await future work.

The next sections contain discussions of the problem of heredity and environment, the methods of attacking it, the factors of heredity and environment as they affect intelligence and the present points of view on personality. A final section, "Position of Modern Psychiatry," is necessarily brief and will probably be of less interest to the psychiatrist than the earlier material on intelligence and personality.

Comprehensive bibliographies which will greatly assist the student follow each major section.

Conclusions on the basis of present findings are, of course, limited, but it is evident that the old general question of the "relative importance of heredity and environment" is no longer valid. New questions must be specific, and determinations must be made of the extent of the variation heredity will permit in a certain psychologic characteristic, given a certain environment, or vice versa. Among the particular results of the survey are many of great interest. Various studies of intelligence, heretofore usually of "general intelligence" rather than of specific intellectual reactions, have shown that environmental differences have less weight than might be supposed. Changes in the social-cultural environment apparently have to be marked, introduced at an early age and prolonged for many years to have much effect on intelligence as shown by tests. Physical interference by ill health, accident or disease seems to have even less influence in most cases. Practically no conclusions can yet be drawn as to the factors of heredity or environment in relation to personality characteristics, but Schwesinger predicts important contributions from the thorough studies of young children which the nursery school now makes possible and which can be followed by repeated studies through adolescence.

Mental Defect. By Lionel S. Penrose, M.A., M.D. Price, $2.50. Pp. 205, with 9 illustrations. New York: Farrar & Rinehart, 1934.

It is ground for satisfaction that this English work should be made available to American readers, as it approaches the problem with emphasis not the same as that of the works with which they are more familiar. In this country the emphasis in mental deficiency has been largely on the psychometric aspects. In this volume a scant 5 per cent of the material bears directly on that topic, a treatment that is of course inadequate from the point of view of the "clinical psychologist." On the other hand, the geneticist will find his field more than amply represented, as will the student of the general somatic aspects of the subject. The earlier portion of the volume is concerned chiefly with methods of investigation, the latter with descriptions of clinical types and, to some extent, with management. The concept of "subcultural amentia" is a happy one. The outlook on sterilization is skeptical. The discussion of mental diseases, like that of psychometrics, is a little sketchy, and while Penrose acclaims Freud as the greatest psychiatrist of modern times, he mentions "two classic forms of dementia praecox" (dementia simplex and dementia praecocissima) as "fairly frequently seen in persons mentally defective." The book will bring most to the layman, the general practitioner and the special student who is already familiar with the psychopathology that it offers but slightly and who needs a fuller perspective of the somatic component of his subject.

Neuroanatomy. By J. H. Globus, B.S., M.D., Associate Professor of Neuropathology and Neuroanatomy, New York University and Bellevue Hospital Medical College. Sixth edition, revised and enlarged. Price, $3.50. Pp. 240, with 89 illustrations. Baltimore: William Wood & Company, 1934.

The sixth edition of this guide for the study of the form and internal structure of the brain and spinal cord appears in a new and enlarged form. The book is arranged in two parts. Part I consists of descriptive text and directions for the student's work, arranged in twenty-three assignments. This is illustrated with thirty-six photomicrographs and semischematic drawings. In part II are fifty-three plates of outline drawings, which the student is to fill in. Instead of the loose-leaf arrangement previously used, the plates are perforated near their attached border, so that they can be taken out when the drawings are being completed. Then they can be reattached by strips of adhesive paper, so that the student has a permanent record of his work. This method of study tends to shorten the time necessary to make records of the structures seen—an important factor in these days of crowded rosters.

Mental Hygiene: Past, Present and Future. By Arthur Hiler Ruggles, M.D., Superintendent, Butler Hospital, Providence, R. I. Price, $1.50. Pp. 104. Baltimore: Williams & Wilkins Company, 1934.

Although this booklet comprises only 104 pages, it contains an exceedingly interesting presentation of the history, development and future of psychiatry and mental hygiene. The material is that of the Colver Lectures of 1932. The booklet is divided into three parts. The first section, "The Mental Health of the Past," gives an excellent summary of the history of psychiatry through ancient times to the development of the hospital period in the latter part of the nineteenth century. The second section, "The Mental Health of the Present," reviews the influences that have made psychiatry a medical specialty. The third section, "The Mental Health of the Future," outlines the possibilities of the growth of psychiatry and shows how the field should develop toward the objectives desired. All this is unusually enjoyable reading and acquaints one thoroughly with how mental health has developed and how important it is to the community.

The Story of Scientific Psychology. By Adelbert Ford. Price, $3. Pp. 307, with 23 illustrations. New York: Sears Publishing Company, Inc., 1932.

Professor Ford's book presents an interesting survey of psychology for the general reader. His discussion of mental testing is poor, however, and several sections of the book suffer because of his prejudice against the psychiatrist.